```
     (FILE 'REGISTRY' ENTERED AT 12:01:19 ON 16 MAR 2001)
                E FIBRONECTIN/CN
L2           47 S FIBRONECTIN ?/CN

     FILE 'CAPLUS' ENTERED AT 12:01:53 ON 16 MAR 2001
L1         3435 SEA FILE=CAPLUS ABB=ON  PLU=ON  (LDL OR LOW?(1W)(LIPOPROT
                EIN OR LIPO PROTEIN))(S)(DETERM? OR DETECT? OR DET## OR
                SCREEN?)
L2           47 SEA FILE=REGISTRY ABB=ON  PLU=ON  FIBRONECTIN ?/CN
L3           12 SEA FILE=CAPLUS ABB=ON  PLU=ON  L1 AND (L2 OR FIBRONECTIN
                )


L1         3435 SEA FILE=CAPLUS ABB=ON  PLU=ON  (LDL OR LOW?(1W)(LIPOPROT
                EIN OR LIPO PROTEIN))(S)(DETERM? OR DETECT? OR DET## OR
                SCREEN?)
L5          880 SEA FILE=CAPLUS ABB=ON  PLU=ON  L1(S)(BLOOD OR PLASMA)
L6          107 SEA FILE=CAPLUS ABB=ON  PLU=ON  L5 AND ANTIBOD?
L7            7 SEA FILE=CAPLUS ABB=ON  PLU=ON  L6 AND ARTERIOSCLER?


L8           18 L3 OR L7

=> d 1-18 .bevstr

L8   ANSWER 1 OF 18  CAPLUS  COPYRIGHT 2001 ACS
ACCESSION NUMBER:         2001:62437  CAPLUS
DOCUMENT NUMBER:          134:97520
TITLE:                    Method for detecting low
                          density lipoprotein (LDL) or
                          denatured LDL in blood
INVENTOR(S):              Uchida, Kazuo; Mashiba, Shinichi
PATENT ASSIGNEE(S):       Ikagaku Co., Ltd., Japan
SOURCE:                   Eur. Pat. Appl., 23 pp.
                          CODEN: EPXXDW
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.        KIND  DATE          APPLICATION NO.  DATE
     ---------------   ----  --------      ---------------  --------
     EP 1070962         A2   20010124      EP 2000-114984   20000720
         R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC,
             PT, IE, SI, LT, LV, FI, RO
PRIORITY APPLN. INFO.:                    JP 1999-207913   19990722
                                          JP 2000-12210    20000120
AB   A novel method for detecting LDL and denatured
     LDL (particularly, oxidized LDL) having a
```

significant concern with the onset and progression of **arteriosclerosis** and Alzheimer's disease is provided, wherein a complex of denatured **LDL** (particularly, oxidized **LDL**) with an acute phase reactant, **blood** coagulation-fibrinolytic-related protein or disinfectant substance produced by macrophage is used as a measuring subject. Human LDL free of .alpha.1 antitrypsin and human **fibronectin** were treated with a copper sulfate soln. at 37.degree. over night to form an oxidized LDL-**fibronectin** complex. The complex was used as an immunogen in a mouse from which monoclonal **antibodies** were prepd. for use in assaying for the complex.

L8 ANSWER 2 OF 18 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2000:769561 CAPLUS
DOCUMENT NUMBER: 133:319287
TITLE: Method for detecting lipoprotein causative of arteriosclerosis, and antibody used for method
INVENTOR(S): Uchida, Ichio; Mashiba, Shinichi
PATENT ASSIGNEE(S): Ikagaku K. K., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 9 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2000304747	A2	20001102	JP 1999-109001	19990416

AB A novel method is provided for **detecting** the lipoprotein causative of arteriosclerosis (e.g., **LDL**-Ig complex, oxidized **LDL**-Ig complex). The lipoprotein causative of arteriosclerosis is detected by a solid phase method upon its adsorption or adhesion onto a macromol. compd. (e.g., polystyrene, nylon, polypropylene, polycarbonate) used as a material for detection, or an extracellular substrate component (e.g., collagen, **fibronectin**, laminin, proteoglycan) used as a solid phase reagent. Alternatively, the lipoprotein causative of arteriosclerosis is **detected** by either enzyme immunoassay, latex agglutination reaction, luminescence immunoassay or immunochromatog. using an antibody specific to **LDL**/IgA complex and an anti-human ApoB antibody labeled with a labeling substance.

L8 ANSWER 3 OF 18 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1999:795994 CAPLUS
DOCUMENT NUMBER: 132:31744
TITLE: Gene probes used for genetic profiling in healthcare screening and planning

INVENTOR(S): Roberts, Gareth Wyn
PATENT ASSIGNEE(S): Genostic Pharma Ltd., UK
SOURCE: PCT Int. Appl., 745 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9964627	A2	19991216	WO 1999-GB1780	19990604

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.:	
GB 1998-12099	19980606
GB 1998-13291	19980620
GB 1998-13611	19980624
GB 1998-13835	19980627
GB 1998-14110	19980701
GB 1998-14580	19980707
GB 1998-15438	19980716
GB 1998-15574	19980718
GB 1998-15576	19980718
GB 1998-16085	19980724
GB 1998-16086	19980724
GB 1998-16921	19980805
GB 1998-17097	19980807
GB 1998-17200	19980808
GB 1998-17632	19980814
GB 1998-17943	19980819

AB There is considerable evidence that significant factor underlying the individual variability in response to disease, therapy and prognosis lies in a person's genetic make-up. There have been numerous examples relating that polymorphisms within a given gene can alter the functionality of the protein encoded by that gene thus leading to a variable physiol. response. In order to bring about the integration of genomics into medical practice and enable design and building of a technol. platform which will enable the everyday practice of mol. medicine a way must be invented for the DNA sequence data to be aligned with the identification of genes central to the induction, development, progression and outcome of disease or physiol. states of interest. According to the invention, the no. of

genes and their configurations (mutations and polymorphisms) needed to be identified in order to provide crit. clin. information concerning individual prognosis is considerably less than the 100,000 thought to comprise the human genome. The identification of the identity of the core group of genes enables the invention of a design for genetic profiling technologies which comprises of the identification of the core group of genes and their sequence variants required to provide a broad base of clin. prognostic information - "genostics". The "Genostic.RTM." profiling of patients and persons will radically enhance the ability of clinicians, healthcare professionals and other parties to plan and manage healthcare provision and the targeting of appropriate healthcare resources to those deemed most in need. The use of this invention could also lead to a host of new applications for such profiling technologies, such as identification of persons with particular work or environment related risk, selection of applicants for employment, training or specific opportunities or for the enhancing of the planning and organization of health services, education services and social services.

L8 ANSWER 4 OF 18 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1999:795993 CAPLUS
DOCUMENT NUMBER: 132:31743
TITLE: Gene probes used for genetic profiling in healthcare screening and planning
INVENTOR(S): Roberts, Gareth Wyn
PATENT ASSIGNEE(S): Genostic Pharma Limited, UK
SOURCE: PCT Int. Appl., 149 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9964626	A2	19991216	WO 1999-GB1779	19990604
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9941586	A1	19991230	AU 1999-41586	19990604
AU 9941587	A1	19991230	AU 1999-41587	19990604
GB 2339200	A1	20000119	GB 1999-12914	19990604

Searcher : Shears 308-4994

PRIORITY APPLN. INFO.:

GB 1998-12098	19980606
GB 1998-28289	19981223
GB 1998-16086	19980724
GB 1998-16921	19980805
GB 1998-17097	19980807
GB 1998-17200	19980808
GB 1998-17632	19980814
GB 1998-17943	19980819
WO 1999-GB1779	19990604

AB There is considerable evidence that significant factor underlying the individual variability in response to disease, therapy and prognosis lies in a person's genetic make-up. There have been numerous examples relating that polymorphisms within a given gene can alter the functionality of the protein encoded by that gene thus leading to a variable physiol. response. In order to bring about the integration of genomics into medical practice and enable design and building of a technol. platform which will enable the everyday practice of mol. medicine a way must be invented for the DNA sequence data to be aligned with the identification of genes central to the induction, development, progression and outcome of disease or physiol. states of interest. According to the invention, the no. of genes and their configurations (mutations and polymorphisms) needed to be identified in order to provide crit. clin. information concerning individual prognosis is considerably less than the 100,000 thought to comprise the human genome. The identification of the identity of the core group of genes enables the invention of a design for genetic profiling technologies.

L8 ANSWER 5 OF 18 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1998:351873 CAPLUS
DOCUMENT NUMBER: 129:25379
TITLE: Kit for measurement of **arteriosclerosis**
INVENTOR(S): Mashiba, Shinichi; Uchida, Kazuo
PATENT ASSIGNEE(S): Kyoto Ikagaku Kenkyusho K. K., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 5 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 10142226	A2	19980529	JP 1996-317162	19961112

AB The kit is used for measurement of modified LDL-.alpha.1-antitrypsin macromol. complex in blood serum or plasma. The kit is useful for immunoassay such as enzyme immunoassay, latex agglutination reaction, and immunochromatog. Modified **LDL** -.alpha.1-antitrypsin macromol. complex in human serum or

plasma was **detd.** by ELISA using monoclonal **antibodies** against human macromol. .alpha.1-antitrypsin.

L8 ANSWER 6 OF 18 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1997:511797 CAPLUS
DOCUMENT NUMBER: 127:203491
TITLE: Cardiovascular determinants of plasma **fibronectin** in an elderly population. The EVA study
AUTHOR(S): Bizbiz, L.; Labat-Robert, J.; Alperovitch, A.; Robert, L.
CORPORATE SOURCE: EVA-Group, Laboratoire Biologie Cellulaire, Universite Paris VII, Paris, 75251, Fr.
SOURCE: Arch. Gerontol. Geriatr. (1997), 25(2), 201-209
CODEN: AGGEDL; ISSN: 0167-4943
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Plasma **fibronectin** was detd. in 1262 individuals (742 females, 520 males) aged 59-71 yr at the beginning of an epidemiol. study on vascular aging (the EVA study) in Nantes, western France. The av. values (62.88.+-.20.30 mg/100 mL for males, n = 520 and 62.15.+-.18.85 mg/100 mL for females, n = 742) and the distribution of values were comparable for males and females. Significant pos. correlations were found in both sexes between plasma **fibronectin** values and some cardiovascular risk factors such as body mass index, systolic and diastolic blood pressure, total and low d. lipoprotein (LDL)-cholesterol, apolipoprotein B, triglycerides and fibrinogen. A significant neg. correlation was found with high d. lipoprotein (HDL)-cholesterol. No correlation was found between **fibronectin** values and smoking or alc. consumption. Multiple regression anal. showed that systolic blood pressure, LDL cholesterol and triglycerides remained significantly assocd. with plasma **fibronectin** whereas only marginal assocns. were found with age, body mass index and fibrinogen. These results are in agreement with previous findings showing a strong increase in **fibronectin** in atherosclerotic plaques and also the complex formation between **fibronectin** and LDL. These results substantiate the claim that modifications of the metab. of extracellular matrix components accompany the atherosclerotic process.

L8 ANSWER 7 OF 18 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1997:87177 CAPLUS
DOCUMENT NUMBER: 126:142855
TITLE: Oxidized LDL stimulates the expression of TGF-.beta. and **fibronectin** in human glomerular epithelial cells
AUTHOR(S): Ding, Guohua; Van Goor, Harry; Ricardo, Sharon

D.; Orlowski, Janis M.; Diamond, Jonathan R.
CORPORATE SOURCE: Department of Medicine, The M. S. Hershey Medical Center, The Pennsylvania State University College of Medicine, Hershey, PA, USA
SOURCE: Kidney Int. (1997), 51(1), 147-154
CODEN: KDYIA5; ISSN: 0085-2538
PUBLISHER: Blackwell
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Abnormal lipid accumulation in glomeruli is a recognized early event in the development of glomerulosclerosis. The presence of LDL and scavenger receptors has recently been demonstrated in glomerular cells, including the visceral epithelial cells. To explore the possible mol. mechanisms of lipid-induced glomerular injury, the present investigation was conducted to examine the effects of oxidized LDL (ox-LDL) on the expression of transforming growth factor (TGF)-.beta. and **fibronectin** by cultured human glomerular epithelial cells (GEC). Cultured GEC were exposed to human ox-LDL (0 to 100 .mu.g/mL) for various time points. Ox-LDL induced a dose- and time-dependent increase in the expression of TGF-.beta. mRNA. Actinomycin D, a transcriptional inhibitor, but not cycloheximide, a protein synthesis inhibitor, inhibited the response. GEC exposed to ox-LDL also demonstrated elevated levels of **fibronectin** mRNA. In addn., treatment of GEC with ox-**LDL** resulted in increased TGF-.beta. and **fibronectin** protein expression as **detected** by immunocytochem. Addn. of anti-TGF-.beta. antibody significantly inhibited the increase in **fibronectin** message level induced by ox-LDL. These data suggest that ox-LDL stimulates matrix protein **fibronectin** in GEC by a mechanism involving expression of TGF-.beta.. Thus, accumulation of lipids in human glomerular epithelial cells may contribute to the pathogenesis of glomerulosclerosis through TGF-.beta. mediated mechanism(s).

L8 ANSWER 8 OF 18 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1996:153511 CAPLUS
DOCUMENT NUMBER: 124:197747
TITLE: **Antibodies** to lipoproteins and apolipoproteins and methods of use thereof
INVENTOR(S): Koren, Eugen; Koscec, Mirna
PATENT ASSIGNEE(S): Oklahoma Medical Research Foundation, USA
SOURCE: PCT Int. Appl., 87 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

Searcher : Shears 308-4994

WO 9600903	A1	19960111	WO 1995-US8331	19950630
W: AU, CA, JP, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
US 6107045	A	20000822	US 1994-268809	19940630
CA 2194163	AA	19960111	CA 1995-2194163	19950630
AU 9530015	A1	19960125	AU 1995-30015	19950630
AU 710945	B2	19990930		
EP 767914	A1	19970416	EP 1995-926157	19950630
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
JP 10507514	T2	19980721	JP 1995-503470	19950630
PRIORITY APPLN. INFO.:			US 1994-268809	19940630
			WO 1995-US8331	19950630

AB Compns. and methods using **antibodies** which are immunoreactive with specific apolipoproteins to **det.** the concns. of lipoproteins such as HDL and **LDL** and/or apolipoproteins in human **blood**, serum, or **plasma** sample are described. Monoclonal **antibodies** (MAbs) are described that specifically bind to epitopes present in apolipoproteins and lipoproteins, enabling rapid and reliable **detns.** of levels of specific **blood** lipoprotein and/or apolipoprotein levels, including Apo B-100, Apo A-I, Apo A-II, Apo C-III, and Apo E, and thereby **detn.** of relative ratios of HDL and **LDL** and LpaI and LpaII. In a preferred embodiment, the compns. are strips of a solid-phase material coated with .gtoreq.1 of the **antibodies** and are referred to herein as "dipsticks". The dipsticks specifically bind a lipoprotein or apolipoprotein when dipped into a protein sample. The amt. of lipid assocd. with a bound lipoprotein or the amt. of apolipoprotein bound on the dipstick is quantitated by using an appropriate method, e.g., by staining with a lipid stain or reaction with a second labeled **antibody**. The intensity of the stain on the dipstick is proportional to the concn. of the lipoprotein lipid or apolipoprotein circulating in the blood and can be quantitated by comparison with stds. contg. known amts. of lipid. The methods are useful in the study of atherosclerosis.

L8 ANSWER 9 OF 18 CAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER:	1995:655524 CAPLUS
DOCUMENT NUMBER:	123:81107
TITLE:	Detection of autoantibodies against oxidized low-density lipoproteins and of IgG-bound low density lipoproteins in patients with coronary artery disease
AUTHOR(S):	Boullier, Agnes; Hamon, Martial; Walters-Laporte, Evelyne; Martin-Nizart, Francoise; Mackereel, Regine; Fruchart,

Jean-Charles; Bertrand, Michel; Duriez, Patrick
CORPORATE SOURCE: Departement d'etudes et de recherches sur les lipoproteines et l'atherosclerose, SERLIA et INSERM U325, Institut Pasteur, Faculte de pharmacie, 1, rue du Professeur Calmette, BP 245, 59019 Lille, Fr.
SOURCE: Clin. Chim. Acta (1995), 238(1), 1-10
CODEN: CCATAR; ISSN: 0009-8981
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The role of oxidized low-d. lipoprotein (ox-LDL) in the pathogenesis of atherosclerosis has been the object of intense investigation. It has been proposed that, due to the antigenic properties of ox-LDL, the anti-ox-LDL **antibody** titer could represent a useful index of in vivo LDL oxidn. LDL immune complexes (LDL-IC) have been demonstrated in patients with coronary disease and could play an atherogenic role. The goal here was to investigate anti-malondialdehyde (MDA)-LDL autoantibodies and LDL-IC in a cohort of patients with coronary artery disease. Control subjects and coronary angiog. documented patients were compared; in addn. healthy male non-smokers were compared with healthy male smokers (>10 cigarettes/day). All patients were matched for age and cholesterolemia. ELISA was used to measure anti-MDA-LDL autoantibodies and LDL-IC. Titers of anti-MDA-LDL autoantibodies were not larger in patients with documented coronary artery stenosis and in smokers than they were in controls and non-smokers. The titer of LDL-IC was not higher in patients with coronary artery stenosis than in controls. Thus, in populations matched for age and cholesterolemia the titers of anti-MDA-LDL autoantibodies and the titer of LDL-IC are not increased in patients suffering from coronary artery stenosis. Furthermore, cigarette smoking does not induce higher titers of anti-MDA-LDL autoantibodies in healthy patients.

L8 ANSWER 10 OF 18 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1995:609915 CAPLUS
DOCUMENT NUMBER: 123:53433
TITLE: Malondialdehyde-modified low density lipoproteins in patients with atherosclerotic disease
AUTHOR(S): Holvoet, Paul; Perez, Graciela; Zhao, Zhian; Brouwers, Els; Bernar, Hilde; Collen, Desire
CORPORATE SOURCE: Center Mol. Vascular Biol., Univ. Leuven, Louvain, B-3000, Belg.
SOURCE: J. Clin. Invest. (1995), 95(6), 2611-19
CODEN: JCINAO; ISSN: 0021-9738
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The murine monoclonal **antibody** mAb-1H11 raised against

malondialdehyde (MDA)-modified **LDL**, was used to **detect** cross-reacting material in human atheromatous tissue and in **plasma**. MDA-modified LDL levels in plasma were 0.19 .+-. 0.02 mg/dL (mean .+-. SEM) in 44 control subjects, 0.24 .+-. 0.02 mg/dL in 15 patients with chronic stable angina pectoris (P = NS vs LDL cholesterol matched controls), 1.4 .+-. 0.1 mg/dL in 60 patients with acute myocardial infarction (P < 0.001 vs controls), and 0.86 .+-. 0.11 mg/dL in 22 patients with carotid atherosclerosis (P < 0.001 vs controls). Modified LDL, isolated from pooled LDL of 10 patients, showed a higher electrophoretic mobility on agarose gels, a higher content of thiobarbituric acid reactive substances, and a higher cholesterol/protein ratio than native LDL and had a similar reactivity (antigen/protein ratio) in the assay as the in vitro MDA-modified LDL used for calibration. Its apo B-100 moiety was not fragmented. Uptake of this modified LDL by macrophages resulted in foam cell generation. In conclusion, elevated plasma levels of atherogenic MDA-modified LDL may be a marker for unstable atherosclerotic cardiovascular disease.

L8 ANSWER 11 OF 18 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1995:544453 CAPLUS
DOCUMENT NUMBER: 123:30622
TITLE: Effect of high glucose on formation of extracellular matrix components by cultured rat heart endothelial cells
AUTHOR(S): Spiro, M.J.; He, Q.; D'Autilia, M.L.
CORPORATE SOURCE: Department of Medicine, Harvard Medical School, Boston, MA, USA
SOURCE: Diabetologia (1995), 38(4), 430-6
CODEN: DBTGAJ; ISSN: 0012-186X
DOCUMENT TYPE: Journal
LANGUAGE: English

AB To define the basis for the microvascular changes obsd. in diabetic myocardium, a study was undertaken on the effect of elevated glucose on the synthesis by rat heart endothelial cells of the extracellular matrix components, types VI, IV and I collagen, as well as **fibronectin**. Confluent cultures of these cells, isolated by fluorescence-activated cell sorting after treatment with rhodamine-labeled acetylated **low**-d. **lipoprotein**, showed a 3-5-fold enhancement in the synthesis of type VI collagen after exposure for 48 h to high glucose (20-30 mM), as **detd**. by immunoblot anal. Increased prodn. of type IV collagen and **fibronectin** was also obsd., but the change was smaller and no effect on type I collagen was found. Measurement of mRNA levels by hybridization with cDNA probes indicated that 48-h exposure to high glucose significantly increased the level of transcripts for type VI and IV collagens but not for type I collagen. While glucose consumption by endothelial cells in high glucose doubled in the initial 24-h period, utilization returned to normal by 48 h,

concomitant with a redn. in GLUT1 transcript levels, suggesting that signals for stimulation of collagen synthesis must be active during the initial period of exposure to elevated glucose levels.

L8 ANSWER 12 OF 18 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1995:386696 CAPLUS
DOCUMENT NUMBER: 122:205957
TITLE: Low-density lipoprotein stimulation of mesangial cell **fibronectin** synthesis: role of protein kinase C and transforming growth factor-.beta.
AUTHOR(S): Studer, Rebecca K.; Craven, Patricia A.; DeRubertis, Frederick R.
CORPORATE SOURCE: VA Medical Center, Pittsburgh, PA, 15240, USA
SOURCE: J. Lab. Clin. Med. (1995), 125(1), 86-95
CODEN: JLCMAK; ISSN: 0022-2143
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Low-d. lipoprotein (LDL) cholesterol has been implicated in the pathogenesis of glomerulosclerosis in diabetes and other forms of glomerular injury. In the present study we evaluated the effect of LDL on **fibronectin** synthesis in cultured rat mesangial cells (MCs) and the roles of protein kinase C (PKC) and transforming growth factor-.beta. (TGF-.beta.) in mediating this LDL action. In MCs, 25 .mu.g to 100 .mu.g/mL LDL increased PKC activity within 15 min, as reflected by enhanced in situ phosphorylation of the 80 kd myristoylated alanine-rich C kinase substrate protein, a specific endogenous substrate of PKC in MC. The same concns. of LDL subsequently (18 to 72 h) enhanced **fibronectin** synthesis, as reflected by increased incorporation of labeled methionine into **fibronectin**. GF 109203X, a selective inhibitor of PKC, blocked increases in both PKC activity and **fibronectin** synthesis induced by LDL in MCs. Furthermore, prior downregulation of PKC to less than 1% of basal activity by exposure of MCs to 0.5 .mu.mol/L phorbol myristate acetate (PMA) also prevented LDL stimulation of **fibronectin** synthesis. The activation of PKC by LDL seen after 15 min of exposure was transient and was not obsd. after 4 or 48 h of exposure of MCs to LDL. However, exposure to LDL for 48 h, but not for 15 min or 4 h, increased both maximal PKC responses to phorbol dibutyrate (PDBu) and tritiated PDBu binding to MCs by 30%. These findings suggest that chronic exposure to LDL increases the total PKC content in MCs and thereby might modulate responses to other PKC agonists. Neither the cyclooxygenase inhibitor piroxicam nor the thromboxane/prostaglandin endoperoxide receptor blocker Sq-29548 altered LDL stimulation of **fibronectin** synthesis in MCs, suggesting that this action of LDL was not mediated by changes in MC eicosanoid generation. By contrast, antibody to TGF-.beta. blocked LDL stimulation of **fibronectin** synthesis in MCs. TGF-.beta. bioactivity,

detd. with the mink lung epithelial cell assay, was two to three times higher in the medium of MCs cultured with **LDL** for 24 to 48 h as compared with corresponding control values. Total TGF-.beta. bioactivity examd. after heat activation of latent TGF-.beta. was also two times higher in the medium of MCs exposed to LDL as compared with that of controls. Prior down-regulation of PKC by exposure of MCs to PMA blocked the increases in TGF-.beta. bioactivity induced by LDL. The results thus implicate both activation of PKC and TGF-.beta. in the expression of the action of LDL to enhance **fibronectin** synthesis in MCs. They suggest that activation of PKC by LDL signals increases in TGF-.beta. bioactivity, which in turn mediates the LDL action to increase **fibronectin** synthesis in MCs.

L8 ANSWER 13 OF 18 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1994:51531 CAPLUS
DOCUMENT NUMBER: 120:51531
TITLE: Low-density lipoprotein oxidation in essential hypertension
AUTHOR(S): Maggi, Elena; Marchesi, Eugenia; Ravetta, Valentina; Falaschi, Francesco; Finardi, Giorgio; Bellomo, Giorgio
CORPORATE SOURCE: 1st Med. Clin., Univ. Pavia, Pavia, Italy
SOURCE: J. Hypertens. (1993), 11(10), 1103-11
CODEN: JOHYD3; ISSN: 0263-6352
DOCUMENT TYPE: Journal
LANGUAGE: English
AB This study investigated the occurrence of enhanced low-d. lipoprotein (LDL) oxidn. as an addnl. factor promoting atherosclerosis progression in hypertensive patients. The oxidn. of plasma LDL was investigated in a group of untreated patients with mild-to-moderate essential hypertension without clin. evident target organ damage and in a group of control subjects. LDL oxidn. was evaluated as both the susceptibility to oxidn. in vitro and the presence of plasma anti-oxidized LDL **antibodies** (as an index for oxidn. in vivo). LDL from hypertensive subjects exhibited enhanced susceptibility to oxidn. in vitro as revealed by early and accelerated generation of conjugated dienes after exposure to CuSO4. Vitamin E concn. in LDL from hypertensive subjects was slightly but significantly decreased and its efficiency in protecting LDL from oxidn. was impaired. Furthermore, a higher plasma anti-oxidized LDL titer was found in hypertensive patients. Subclass anal. revealed that the contemporary presence of hypercholesterolemia did not modify either the increased susceptibility of **LDL** to oxidn. or the presence of **plasma** antioxidized **LDL antibodies detected** in hypertensive patients. Moreover, no correlation was found between LDL oxidn. parameters and blood pressure values. Thus, LDL from hypertensive patients is more susceptible to oxidn. in vitro and is more promptly oxidized in

vivo. These findings suggest a possible participation of LDL oxidn. in promoting and accelerating the atherosclerosis that often develops in hypertensive patients.

L8 ANSWER 14 OF 18 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1993:446877 CAPLUS
DOCUMENT NUMBER: 119:46877
TITLE: **Plasma** triglycerides **determine** **low** density **lipoprotein** composition, physical properties, and cell-specific binding in cultured cells
AUTHOR(S): McKeone, Barry J.; Patsch, Josef R.; Pownall, Henry J.
CORPORATE SOURCE: Dep. Intern. Med., Baylor Coll. Med., Houston, TX, 77030, USA
SOURCE: J. Clin. Invest. (1993), 91(5), 1926-33
CODEN: JCINAO; ISSN: 0021-9738
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The relationship between the plasma triglycerides and the LDL triglycerides of 30 normal and 48 hypertriglyceridemic subjects has been quantified; the data fit a simple adsorption isotherm, LDL triglyceride/(LDL triglyceride + LDL cholesterol ester) = 0.65 plasma triglyceride/(464 + plasma triglyceride). In vitro transfer of triglyceride from concd. VLDL to VLDL-depleted plasma produced triglyceride-rich LDL that had similar properties. LDL uptake by HepG2 cells increased with LDL triglyceride content whereas the reverse was found with skin fibroblasts. At 37 .degree.C, the cores of both normal and hypertriglyceridemic LDL were isotropic liqs. Circular dichroic spectra revealed no difference in the secondary structure of normal and triglyceride-rich LDL. The affinity of monoclonal **antibody** MB47, which binds to the receptor ligand of apo B-100 was independent of LDL triglyceride content. MB3, which binds near residue 1022 of apo B-100, showed a triglyceride-dependent decrease in affinity for LDL from hypertriglyceridemic subjects and from in vitro incubations. LDL with an elevated triglyceride content formed in vitro had reduced proteolytic cleavage of apo B-100 by Staphylococcus aureus V9 protease. From these data, the authors infer that (a) **LDL** triglyceride is a predictable function of **plasma** triglyceride, (b) triglyceride induces subtle changes in apo B-100 structure at a site that is remote from the putative receptor binding ligand, and (c) the triglyceride-dependent receptor-binding **determinants** of apo B-100 are recognized differently by fibroblasts and HepG2 cells.

L8 ANSWER 15 OF 18 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1991:457116 CAPLUS
DOCUMENT NUMBER: 115:57116

TITLE: Detection of surface-adsorbed (lipo)proteins by means of a two-step enzyme-immunoassay: a study on the Vroman effect
AUTHOR(S): Poot, A.; Beugeling, T.; Van Aken, W. G.; Bantjes, A.
CORPORATE SOURCE: Dep. CT, Univ. Twente, Enschede, 7500 AE, Neth.
SOURCE: J. Biomed. Mater. Res. (1990), 24(8), 1021-36
CODEN: JBMRBG; ISSN: 0021-9304
DOCUMENT TYPE: Journal
LANGUAGE: English

AB In view of reports on the involvement of high-mol.-wt. (HMW) kininogen and high-d. lipoprotein (HDL) in the Vroman effect, the adsorption of fibrinogen, HMW kininogen, HDL and several other proteins was studied from pooled human plasma and congenitally HMW kininogen-deficient plasma onto glass and low-d. polyethylene, both as a function of the plasma concn. and the contact time. Mixts. of purified (lipo)proteins were also included in the study. Protein adsorption was detd. by means of a two-step enzyme-immunoassay. The results support the hypothesis that HMW kininogen is involved in the displacement of fibrinogen, which is almost instantly adsorbed from normal plasma onto glass. On hydrophobic polymers like polyethylene, the low amts. of adsorbed fibrinogen and HMW kininogen from plasma and concd. plasma solns. may be due to a preferential adsorption of HDL.

L8 ANSWER 16 OF 18 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1988:35297 CAPLUS
DOCUMENT NUMBER: 108:35297
TITLE: Effect of extracellular matrix components on lipid accumulation in human cells
AUTHOR(S): Kotelyanskii, V. E.; Orekhov, A. N.; Tertov, V. V.; Khashimov, Kh. A.; Glukhova, M. A.; Frid, M. G.; Ornatskaya, O. I.; Vasilevskaya, T. D.; Smirnov, V. N.
CORPORATE SOURCE: Cardiol. Res. Cent., Moscow, USSR
SOURCE: Byull. Eksp. Biol. Med. (1987), 104(11), 562-4
CODEN: BEBMAE; ISSN: 0365-9615
DOCUMENT TYPE: Journal
LANGUAGE: Russian

AB The effect of extracellular matrix components on cholesterol accumulation in different human cells was studied. Insol. **low**-d. **lipoprotein** (**LDL**)-heparin-**fibronectin**-gelatin complexes were incubated with human cells (fibroblasts; monocytes; peritoneal macrophages; and aortic wall endothelial, subendothelial intimal, and medial cells), and total cholesterol content in these cells was **detd**. Components of extracellular matrix being complexed with LDL enhanced total cholesterol accumulation in all cell types studied; the highest amt. of cholesterol was accumulated by subendothelial

intimal cells and peritoneal macrophages. It is suggested that components of extracellular matrix can play an important role in the development of lipid-laden foam cells that are accumulated in the arterial wall in atherosclerotic lesions.

L8 ANSWER 17 OF 18 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1987:47840 CAPLUS
DOCUMENT NUMBER: 106:47840
TITLE: Effect of thrombin modification of low-density lipoproteins on their interaction with **fibronectin**
AUTHOR(S): Chulkova, T. M.
CORPORATE SOURCE: Inst. Biol. Med. Chem., Moscow, USSR
SOURCE: Vopr. Med. Khim. (1986), 32(6), 70-3, 1 plates
CODEN: VMDKAM; ISSN: 0042-8809
DOCUMENT TYPE: Journal
LANGUAGE: Russian
AB Interaction of native and thrombin-modified human low-d. lipoproteins (LDL) with immobilized homologous **fibronectin** (either covalently bound to Sepharose or adsorbed from blood serum on collagen-Sepharose) was studied. Treatment of **LDL** with thrombin at pH 7.5 and 37.degree. within 60 min (thrombin/apo B ratio 1 : 20) led to formation in **LDL** prepns. of 3 new fragments of apoprotein B which were **detected** by polyacrylamide gel electrophoresis in presence of SDS. Chromatog. of native and thrombin modified LDL on **fibronectin** -Sepharose showed that 30% of the modified LDL and 2% of native LDL were bound to fibronetin-Sepharose at physiol. pH values and NaCl concns. Study of the interaction of LDL with **fibronectin** adsorbed on collagen-Sepharose showed that thrombin-treated LDL partially released **fibronectin** from the sorbent due to the formation of a modified LDL-**fibronectin** complex. Native LDL did not act in a similar manner. Complexes of modified **LDL** with **fibronectin** were **detected** under conditions of both electrophoresis in 3% polyacrylamide gel and immunoelectrophoresis. Interaction of **LDL** with **fibronectin** may promote accumulation of lipoproteins in he vascualr wall and thus may serve as a model system for evaluation of the extent of atherogeneity of **LDL** and **detection** of the modified **LDL** in vivo.

L8 ANSWER 18 OF 18 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1985:556664 CAPLUS
DOCUMENT NUMBER: 103:156664
TITLE: Demonstration of receptor binding of two apo-B containing lipoproteins by differential labeling with colloidal gold
AUTHOR(S): Hesz, A.; Robenek, H.; Ingolic, E.; Roscher, A.; Krempler, F.; Sandhofer, F.; Kostner, G. M.

CORPORATE SOURCE: Inst. Pathol., Univ. Hosp., Keczkemet, Hung.
SOURCE: Eur. J. Cell Biol. (1985), 37, 229-33
CODEN: EJCBDN; ISSN: 0171-9335
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The interaction of two types of apolipoprotein B (apo-B) contg. lipoproteins, human low-d. lipoprotein (LDL) and lipoprotein-a (Lp(a)), with cultured human skin fibroblasts was studied by differential colloidal Au labeling in conjunction with thin sectioning and surface replication techniques. After sep. exposure of the fibroblasts to either Au labeled LDL or Lp(a) for 15 to 30 min at 37.degree., labeled lipoproteins were predominantly found in coated pit areas. Excess of unlabeled LDL or Lp(a) completely displaced the Au-labeled lipoproteins, indicating specific binding by the LDL-receptor. Simultaneous exposure of fibroblasts to LDL-16 nm Au and Lp(a)-40 nm Au conjugates revealed that both LDL and Lp(a) are bound in the same coated pit and internalized into the same endosome. In contrast to native lipoproteins, Au labeled acetylated lipoproteins were found diffusely distributed on membrane surface areas predominantly representing **fibronectin**-contg. fibrils.

(FILE 'MEDLINE, BIOSIS, EMBASE, WPIDS, CONFSCI, SCISEARCH, JICST-EPLUS, JAPIO' ENTERED AT 12:22:26 ON 16 MAR 2001)

L11 103 S L3
L12 25 S L11 AND ANTIBOD?
L13 7 S L11 AND ARTERIOSCLER?
L14 25 S L11 AND (APO# OR APOLIPOPROTEIN)
L15 47 S L12 OR L13 OR L14
L16 24 DUP REM L15 (23 DUPLICATES REMOVED)

L16 ANSWER 1 OF 24 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD
ACCESSION NUMBER: 2001-125962 [14] WPIDS
DOC. NO. NON-CPI: N2001-092845
DOC. NO. CPI: C2001-036754
TITLE: **Detecting low** density **lipoprotein** (**LDL**) in blood, useful for diagnosis of **arteriosclerosis**, by measuring a complex of **LDL** or denatured **LDL** with an acute phase reactant or a fibrinolytic related protein.
DERWENT CLASS: B04 D16 S03
INVENTOR(S): MASHIBA, S; UCHIDA, K
PATENT ASSIGNEE(S): (IKAG-N) IKAGAKU CO LTD
COUNTRY COUNT: 25
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG

EP 1070962 A2 20010124 (200114)* EN 23
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
EP 1070962	A2	EP 2000-114984	20000720

PRIORITY APPLN. INFO: JP 2000-12210 20000120; JP 1999-207913 19990722

AN 2001-125962 [14] WPIDS

AB EP 1070962 A UPAB: 20010312
NOVELTY - A novel method for **detecting low** density **lipoprotein** (**LDL**) and denatured **LDL** in blood using as a measuring subject a complex of **LDL** or denatured **LDL** (containing oxidized **LDL**) with an acute phase reactant, blood coagulation protein, fibrinolytic related protein or disinfectant substance produced by macrophage. The **LDL** in the complex is not oxidatively denatured.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) a method for detecting a novel lipoprotein concerning **arteriosclerotic** lesion using an antihuman fibrinogen **antibody** and an immune reaction detecting reagent such as an antihuman **ApoB antibody** labeled with a labeling substance, typically including an enzyme; and

(2) a monoclonal **antibody** produced from a hybridoma obtained by fusing a mouse myeloma cell with a spleen cell from mammals immunized with a LDL/**fibronectin** complex, where the **antibody** does not react with native **fibronectin** and **ApoB** (native and denatured **ApoB**) and specifically recognizes a LDL/**fibronectin** complex.

USE - The method can be used for **detecting low** density **lipoprotein** (**LDL**). It can also be used for **detecting** a novel lipoprotein concerning **arteriosclerotic** lesion (all claimed). The methods can be used for early diagnosis of **arteriosclerosis** and Alzheimer's disease, and for drug efficacy evaluation in administering an **arteriosclerosis** treating agent.
Dwg.0/7

L16 ANSWER 2 OF 24 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD
ACCESSION NUMBER: 2001-127686 [14] WPIDS
DOC. NO. NON-CPI: N2001-094253
Searcher : Shears 308-4994

DOC. NO. CPI: C2001-037659
TITLE: Detecting **arteriosclerosis** inducing lipoprotein for diagnosis of various circulatory diseases like cardiac infarction, involves adsorbing high molecular compounds on solid phase reagent having substrate component.
DERWENT CLASS: A96 B04 D16 S03
PATENT ASSIGNEE(S): (KOBE-N) KOBE IKAGAKU KENKYUSHO KK
COUNTRY COUNT: 1
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
JP 2000304747 A		20001102	(200114)*		9

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
JP 2000304747 A		JP 1999-109001	19990416

PRIORITY APPLN. INFO: JP 1999-109001 19990416
AN 2001-127686 [14] WPIDS
AB JP2000304747 A UPAB: 20010312
NOVELTY - Detecting an **arteriosclerosis** inducing lipoprotein involves adsorbing and adhering a detection material containing high molecular compounds like polystyrene, nylon, polypropylene and/or polycarbonate on a solid phase reagent containing an extracellular substrate component like collagen, **fibronectin**, laminin or proteoglycans, by solid phase technique.

DETAILED DESCRIPTION - An INDEPENDENT CLAIM is also included for a monoclonal **antibody** which does not react to native IgA or native **ApoB** but recognizes a LDL/IgA composite specifically, is produced by a hybridoma which is obtained by uniting and immunizing a mouse myeloma cell and a mammalian spleen cell with the LDL/IgA composite.

USE - For diagnosis of various circulatory diseases such as cardiac infarction, angina, cerebral infarction, renal arterial diseases and erosion artery diseases.

ADVANTAGE - The process which effectively **detects** the **arteriosclerosis** inducing lipoprotein and measures the oxidized or unoxidized **LDL** and immunoglobin, is also used in the diagnosis of cerebrovascular dementia and diabetic nephropathy.

Dwg.0/5

L16 ANSWER 3 OF 24 BIOSIS COPYRIGHT 2001 BIOSIS DUPLICATE 1
Searcher : Shears 308-4994

ACCESSION NUMBER: 2000:489601 BIOSIS
DOCUMENT NUMBER: PREV200000489722
TITLE: Characterization of the basis of lipoprotein (a) lysine-binding heterogeneity.
AUTHOR(S): Xia, Jiazhi; May, Lorraine F.; Koschinsky, Marlys L. (1)
CORPORATE SOURCE: (1) Department of Biochemistry, Queen's University, Kingston, ON, K7L 3N6 Canada
SOURCE: Journal of Lipid Research, (October, 2000) Vol. 41, No. 10, pp. 1578-1584. print.
ISSN: 0022-2275.
DOCUMENT TYPE: Article
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Although elevated plasma concentrations of lipoprotein (a) (Lp(a)) are considered to be a risk factor for atherosclerosis, the mechanisms by which Lp(a) mediates its pathogenic effects have not been conclusively **determined**. The **apolipoprotein** (a) (**apo**(a)) component of Lp(a) confers unique structural properties to this lipoprotein, including the ability to bind to lysine residues in biological substrates. It has been shown, however, that only a fraction of plasma Lp(a) (Lp(a)-Lys+) binds to lysine-Sepharose in vitro. The nature of the non-lysine-binding Lp(a) fraction in plasma (Lp(a)-Lys-) is currently unknown. In the present study, the Lp(a)-Lys+ fraction was **determined** in the plasma of six unrelated individuals; the Lp(a)-Lys+ fraction in these plasma samples ranged from apprx37 to apprx48%. Interestingly, purification of the Lp(a) by density gradient ultracentrifugation followed by gel filtration and ion-exchange chromatography resulted in progressive increases in the Lp(a)-Lys+ fraction. Addition of either purified **low** density **lipoprotein** (**LDL**) or **fibronectin** to the purified Lp(a) at a 1:1 molar ratio reduced the Lp(a)-Lys+ fraction (maximal decrease of 34 and 20%, respectively) whereas addition of both **fibronectin** and **LDL** to the purified Lp(a) resulted in a further decrease (45% maximally) in this fraction. Similar results were obtained by using a recombinant expression system for **apo**(a): addition of a 4-fold molar excess of either **LDL** or **fibronectin** to conditioned medium containing metabolically labeled recombinant **apo**(a) reduced the Lys+ fraction by 49 and 23%, respectively. Taken together, our data suggest that the lysine-binding heterogeneity of plasma Lp(a) is not primarily an intrinsic property of the lipoprotein, but rather results in large part from its ability to noncovalently associate with abundant plasma components such as **LDL** and **fibronectin**. These interactions appear to mask the lysine-binding site in **apo**(a) kringle IV type 10, which mediates the interaction of Lp(a) with lysine-Sepharose. The contribution of these interactions to the function of Lp(a) in vivo remains to be investigated.

L16 ANSWER 4 OF 24 SCISEARCH COPYRIGHT 2001 ISI (R)
ACCESSION NUMBER: 2000:809311 SCISEARCH
THE GENUINE ARTICLE: 366UG
TITLE: Donor origin of circulating endothelial progenitors after allogeneic bone marrow transplantation
AUTHOR: Ikpeazu C; Davidson M K; Halteman D; Goodman S A; Browning P J; Brandt S J (Reprint)
CORPORATE SOURCE: VANDERBILT UNIV, MED CTR, DIV HEMATOL ONCOL, BONE MARROW TRANSPLANT PROGRAM, ROOM 547 MRB 2, NASHVILLE, TN 37232 (Reprint); VANDERBILT UNIV, MED CTR, DIV HEMATOL ONCOL, BONE MARROW TRANSPLANT PROGRAM, NASHVILLE, TN 37232; VANDERBILT UNIV, MED CTR, DEPT MED, NASHVILLE, TN 37232; VANDERBILT UNIV, MED CTR, DEPT CELL BIOL, NASHVILLE, TN 37232; VANDERBILT UNIV, MED CTR, VANDERBILT INGRAM CANC CTR, NASHVILLE, TN 37232; NASHVILLE VET AFFAIRS MED CTR, NASHVILLE, TN
COUNTRY OF AUTHOR: USA
SOURCE: BIOLOGY OF BLOOD AND MARROW TRANSPLANTATION, (JAN 2000) Vol. 6, No. 3A, pp. 301-308.
Publisher: CARDEN JENNINGS PUBL CO LTD, BLAKE CTR, STE 200, 1224 W MAIN ST, CHARLOTTESVILLE, VA 22903.
ISSN: 1083-8791.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: CLIN
LANGUAGE: English
REFERENCE COUNT: 45

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Endothelial cell precursors circulate in blood and express antigens found on hematopoietic stem cells, suggesting that such precursors might be subject to transplantation. To investigate, we obtained adherence-depleted peripheral blood mononuclear cells from 3 individuals who had received a sex-mismatched allogeneic bone marrow transplant (BMT) and cultured the cells on **fibronectin**-coated plates with endothelial growth factors. The phenotype of the spindle-shaped cells that emerged in culture was characterized by immunofluorescent staining, and the origin of the cells was **determined** using a polymerase chain reaction (PCR)-based assay for polymorphic short tandem repeats (STRs). The cells manifested a number of endothelial characteristics-such as von Willebrand factor, CD31, and Flk-1/KDR expression; Bandeiraea simplicifolia lectin 1 binding; and acetylated **low**-density **lipoprotein** uptake-but lacked expression of certain markers of activation or differentiation, including intercellular adhesion molecule-1, vascular cell adhesion molecule-1, and the epitope for the anti-endothelial cell **antibody** P1H12. For each patient and at all time points studied (ranging from 5 to 52 months after transplantation), STR-PCR analysis showed that cultured cells and

nucleated blood cells came exclusively from the bone marrow donor. These results demonstrate that circulating endothelial progenitors are both transplantable and capable of long-term repopulation of human allogeneic BMT recipients.

L16 ANSWER 5 OF 24 MEDLINE
ACCESSION NUMBER: 2000027755 MEDLINE
DOCUMENT NUMBER: 20027755
TITLE: Sphingomyelinase, an enzyme implicated in atherogenesis, is present in atherosclerotic lesions and binds to specific components of the subendothelial extracellular matrix.
AUTHOR: Marathe S; Kuriakose G; Williams K J; Tabas I
CORPORATE SOURCE: Departments of Medicine and Anatomy & Cell Biology, Columbia University, New York, NY 10032, USA.
CONTRACT NUMBER: HL56984 (NHLBI)
SOURCE: ARTERIOSCLEROSIS, THROMBOSIS, AND VASCULAR BIOLOGY, (1999 Nov) 19 (11) 2648-58.
Journal code: B89. ISSN: 1079-5642.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200002
ENTRY WEEK: 20000204
AB Atherosclerotic lesions contain an extracellular sphingomyelinase (SMase) activity that hydrolyzes the sphingomyelin of subendothelial **low** density **lipoprotein** (**LDL**). This SMase activity may promote atherosclerosis by enhancing subendothelial **LDL** retention and aggregation, foam cell formation, and possibly other atherogenic processes. The results of recent cell-culture studies have led to the hypothesis that a specific molecule called secretory SMase (S-SMase) is responsible for the SMase activity known to be in lesions, although its presence in atheromata had not been examined directly. Herein we provide immunohistochemical and biochemical support for this hypothesis. First, 2 different **antibodies** against S-SMase **detected** extracellular immunoreactive protein in the intima of mouse, rabbit, and human atherosclerotic lesions. Much of this material in lesions appeared in association with the subendothelial matrix. Second, binding studies in vitro demonstrated that (125)I-S-SMase adheres to the extracellular matrix of cultured aortic smooth muscle and endothelial cells, specifically to the laminin and collagen components. Third, in its bound state, S-SMase retains substantial enzymatic activity against lipoprotein substrates. Overall, these data support the hypothesis that S-SMase is an extracellular arterial wall SMase that contributes to the hydrolysis of the sphingomyelin of subendothelial **LDL**. S-SMase may therefore be an important participant in atherogenesis

through local enzymatic effects that stimulate subendothelial retention and aggregation of atherogenic lipoproteins.

L16 ANSWER 6 OF 24 SCISEARCH COPYRIGHT 2001 ISI (R)
ACCESSION NUMBER: 1999:163349 SCISEARCH
THE GENUINE ARTICLE: 168GQ
TITLE: Blocking very late antigen-4 integrin decreases leukocyte entry and fatty streak formation in mice fed an atherogenic diet
AUTHOR: Shih P T (Reprint); Brennan M L; Vora D K; Territo M C; Strahl D; Elices M J; Lusis A J; Berliner J A
CORPORATE SOURCE: UNIV CALIF LOS ANGELES, SCH MED, DEPT PATHOL & LAB MED, HLTH SCI CTR, 10833 LE CONTE AVE, LOS ANGELES, CA 90095 (Reprint); UNIV CALIF LOS ANGELES, DEPT PATHOL, LOS ANGELES, CA 90095; UNIV CALIF LOS ANGELES, DEPT MED, LOS ANGELES, CA 90095; CYTEL CORP, SAN DIEGO, CA 92121
COUNTRY OF AUTHOR: USA
SOURCE: CIRCULATION RESEARCH, (19 FEB 1999) Vol. 84, No. 3, pp. 345-351.
Publisher: LIPPINCOTT WILLIAMS & WILKINS, 227 EAST WASHINGTON SQ, PHILADELPHIA, PA 19106.
ISSN: 0009-7330.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE
LANGUAGE: English
REFERENCE COUNT: 43

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Atherosclerotic lesion development is characterized by the recruitment of leukocytes, principally monocytes, to the vessel wall. Considerable interest has been focused on the adhesion molecule(s) involved in leukocyte/endothelial interactions. The goal of the present study was to **determine** the role of the very late antigen-4 (VLA-4) integrin/ligand interaction in fatty streak development using murine models. Because alpha 4 null mice are not viable, a peptidomimetic was used to block VLA-4-mediated leukocyte binding. The ability of a synthetic peptidomimetic of connecting segment-1 (CS-1 peptide) to block the recruitment of leukocytes and the accumulation of lipid in the aortic sinus of either wild-type mice (strain C57BL/6J) or mice with a **low**-density **lipoprotein** null mutation (LDLR -/-) maintained on an atherogenic diet was assessed, The active (Ac) CS-1 peptide or scrambled (Sc) CS-I peptide was delivered subcutaneously into mice using a mini osmotic pump. Mice were exposed to the peptide for 24 to 36 hours before the onset of the atherogenic diet. In C57BL/6J mice, leukocyte entry into the aortic sinus, as assessed by en face preparations, was inhibited by the active peptide (Ac=28+/-4, Sc=54+/-6 monocytes/valve; P=0.004). Additionally, frozen sections stained with Oil Red O were analyzed to assess lipid accumulation in

the aortic sinus. C57BL/6J mice that received the (Ac) compound demonstrated significantly reduced lesion areas as compared with mice that received the (Sc) peptide (Ac=4887+/-4438 mu m(2), Sc=15009+/-5619 mu m(2); P<0.0001). In a separate study, LDLR-/- mice were implanted with pumps containing either the (Ac) or (Sc) peptide before initiation of the atherogenic diet. Because LDLR-/- mice fed a chow diet displayed small lesions at 14 weeks, the effects of the peptide seen in these animals represented a change in early lipid accumulation rather than initiation. By using whole-mount preparations, the (Ac) but not the (Sc) peptide significantly reduced the area of lipid accumulation in the aortic sinus, resulting in an approximate 66% decrease. plasma analysis from all studies revealed concentrations of peptide to be present at levels previously **determined** by in vitro analysis to block adhesion. (Ac) CS-1 peptide, which blocks VLA-4 on the leukocyte surface, is effective in reducing leukocyte recruitment and lipid accumulation in the aortic sinus. The present study provides in vivo evidence that the VLA-4 integrin plays an important role in the initiation of the atherosclerotic lesion and lipid accumulation, and it suggests a potential therapeutic strategy for this disease.

L16 ANSWER 7 OF 24 MEDLINE
ACCESSION NUMBER: 1999164822 MEDLINE
DOCUMENT NUMBER: 99164822
TITLE: [**Fibronectin** and diabetes mellitus: the factors that influence its plasma concentrations and its usefulness as a marker of late complications]. Fibronectina y diabetes mellitus: factores que influyen en las concentraciones plasmaticas y utilidad como marcador de complicaciones tardias.
AUTHOR: Simo R; Segura R M; Garcia-Pascual L; Masmiquel L; Burgos R; Hernandez C; Marti R; Mesa J
CORPORATE SOURCE: Seccion de Endocrinologia, Hospital General Vall d'Hebron, Barcelona.
SOURCE: MEDICINA CLINICA, (1999 Jan 23) 112 (2) 45-50. Journal code: LTQ. ISSN: 0025-7753.
PUB. COUNTRY: Spain
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: Spanish
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199905
ENTRY WEEK: 19990503
AB BACKGROUND: The usefulness of plasma **fibronectin** (FNp) as a marker of late diabetic complications is controversial. The aim of the study was to assess the influence of several variables on FNp in diabetic patients and to **determine** its usefulness as a marker of late diabetic complications. PATIENTS AND METHODS: 79 diabetic patients randomly selected were included in the study. The clinical variables considered were: age, gender, body mass index

(BMI), tobacco and alcohol consumption, type, duration and treatment of diabetes, hypertension, and diabetic late complications (macroangiopathy, retinopathy, nephropathy and neuropathy). The laboratory variables analyzed were: blood glucose, glycated hemoglobin, total cholesterol, HDL-cholesterol, **LDL** -cholesterol, trygliceride**s**, **apolipoprotein** AI, **apolipoprotein** B, microalbuminuria, creatinin and FNp. Statistical study included a multiple regression analysis taking FNp as the dependent variable. RESULTS: A direct correlation between FNp and BMI and also with trygliceride**s** was observed ($r = 0.362$; $p = 0.002$, and $r = 0.234$; $p = 0.038$, respectively). Higher levels of FNp were found in type 2 diabetic patients in comparison with type 1 (464 [SD, 127] versus 395 [SD, 96] mg/dl; $p = 0.014$). This difference was due to the higher BMI and trygliceride**s** concentrations observed in type 2 diabetic patients in comparison with type 1 (28.61 [SD, 4.67] versus 22.56 [SD, 2,.19] kg/m2; $p < 0.001$, and 4.24 [SD, 2.36] versus 2.52 [SD, 1.40] mmol/l, respectively). Multiple regression analysis showed that only BMI significantly influenced on FNp concentrations ($r = 0.330$; $p = 0.004$). No relation among FNp and late diabetic complications and other variables considered in the study was observed. CONCLUSIONS: FNp is not a useful marker of diabetic late complications and its concentrations are direct and independently influenced by BMI.

L16 ANSWER 8 OF 24 BIOSIS COPYRIGHT 2001 BIOSIS DUPLICATE 2
ACCESSION NUMBER: 1997:387659 BIOSIS
DOCUMENT NUMBER: PREV199799686862
TITLE: Cardiovascular determinants of plasma **fibronectin** in an elderly population. The EVA study.
AUTHOR(S): Bizbiz, L.; Labat-Robert, J.; Alperovitch, A.; Robert, L. (1)
CORPORATE SOURCE: (1) Lab. Biol. Cellul., Universite Paris VII, tour 23/33, case 7128 ler etage, 2 place Jussieu, 75251 Paris Cedex 05 France
SOURCE: Archives of Gerontology and Geriatrics, (1997) Vol. 25, No. 2, pp. 201-209.
ISSN: 0167-4943.
DOCUMENT TYPE: Article
LANGUAGE: English

AB Plasma **fibronectin** was **determined** in 1262 individuals (742 females, 520 males) aged 59-71 years at the beginning of an epidemiological study on vascular aging (the EVA study) in Nantes, western France. The average values (62.88 +- 20.30 mg/100 ml for males, n= 520 and 62.15 +- 18.85 mg/100 ml for females, n= 742) and the distribution of values were comparable for males and females. Significant positive correlations were found in both sexes between plasma **fibronectin** values and some cardiovascular risk factors such as body mass index, systolic and

diastolic blood pressure, total and **low** density **lipoprotein** (**LDL**)-cholesterol, **apolipoprotein** B, triglycerides and fibrinogen. A significant negative correlation was found with high density lipoprotein (HDL)-cholesterol. No correlation was found between **fibronectin** values and smoking or alcohol consumption. Multiple regression analysis showed that systolic blood pressure, **LDL** cholesterol and triglycerides remained significantly associated with plasma **fibronectin** whereas only marginal associations were found with age, body mass index and fibrinogen. These results are in agreement with previous findings showing a strong increase in **fibronectin** in atherosclerotic plaques and also the complex formation between **fibronectin** and **LDL**. These results substantiate the claim that modifications of the metabolism of extracellular matrix component; accompany the atherosclerotic process.

L16 ANSWER 9 OF 24 MEDLINE DUPLICATE 3
ACCESSION NUMBER: 97148903 MEDLINE
DOCUMENT NUMBER: 97148903
TITLE: Oxidized LDL stimulates the expression of TGF-beta and **fibronectin** in human glomerular epithelial cells.
AUTHOR: Ding G; van Goor H; Ricardo S D; Orlowski J M; Diamond J R
CORPORATE SOURCE: Department of Medicine, M.S. Hershey Medical Center, Pennsylvania State University College of Medicine, Hershey, USA.
SOURCE: KIDNEY INTERNATIONAL, (1997 Jan) 51 (1) 147-54. Journal code: KVB. ISSN: 0085-2538.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199706
ENTRY WEEK: 19970601
AB Abnormal lipid accumulation in glomeruli is a recognized early event in the development of glomerulosclerosis. The presence of **LDL** and scavenger receptors has recently been demonstrated in glomerular cells, including the visceral epithelial cells. To explore the possible molecular mechanisms of lipid-induced glomerular injury, the present investigation was conducted to examine the effects of oxidized **LDL** (ox-**LDL**) on the expression of transforming growth factor (TGF)-beta and **fibronectin** by cultured human glomerular epithelial cells (GEC). Cultured GEC were exposed to human ox-**LDL** (0 to 100 micrograms/ml) for various time points. Ox-**LDL** induced a dose- and time-dependent increase in the expression of TGF-beta mRNA. Actinomycin D, a transcriptional inhibitor, but not

cycloheximide, a protein synthesis inhibitor, inhibited the response. GEC exposed to ox-**LDL** also demonstrated elevated levels of **fibronectin** mRNA. In addition, treatment of GEC with ox-**LDL** resulted in increased TGF-beta and **fibronectin** protein expression as **detected** by immunocytochemistry. Addition of anti-TGF-beta **antibody** significantly inhibited the increase in **fibronectin** message level induced by ox-**LDL**. These data suggest that ox-**LDL** stimulates matrix protein **fibronectin** in GEC by a mechanism involving expression of TGF-beta. Thus, accumulation of lipids in human glomerular epithelial cells may contribute to the pathogenesis of glomerulosclerosis through TGF-beta mediated mechanism(s).

L16 ANSWER 10 OF 24 MEDLINE DUPLICATE 4
ACCESSION NUMBER: 97406569 MEDLINE
DOCUMENT NUMBER: 97406569
TITLE: The role of oxidative stress in the long-term glycation of LDL.
AUTHOR: Menzel E J; Sobal G; Staudinger A
CORPORATE SOURCE: Institute of Immunology, Vienna, Austria.
SOURCE: BIOFACTORS, (1997) 6 (2) 111-24.
Journal code: AEB. ISSN: 0951-6433.
PUB. COUNTRY: Netherlands
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199712
ENTRY WEEK: 19971203

AB Advanced glycation is a major pathway for the posttranslational modification of plasma and tissue proteins. The initiating reaction is the nonenzymatic addition of sugars such as glucose to the primary amino groups of proteins, i.e., mainly to lysine residues. These "early" Schiff base and Amadori products then undergo a series of inter- and intramolecular rearrangements to produce the "late" products termed advanced glycation end products (AGEs). Incubation of **LDL** with glucose or glucose-6-phosphate produces AGE moieties on both the lipid and **apolipoprotein** B components. In addition, we tried to generate AGE-**LDL** by reaction with AGE-peptides (< 10 kD) obtained by enzymatic digestion of long-term glycated **fibronectin** as a model for connective tissue AGE-peptides. AGE-formation can be assessed by monitoring of fluorescence (370/440 nm) which is easily differentiated from the much lower autofluorescence of oxidized **low** density **lipoproteins** (oxLDL). Alternatively, AGE formation was **detected** by an AGE-specific ELISA using **antibodies** elicited in rabbits against bovine AGE-RNAse. In the present study we investigated the influence of oxidative stress on the long-term glycation of **LDL** and the modulation of

LDL-oxidation by AGE-modification. We observed (a) that the rate of AGE formation is reduced by BHT/EDTA both on **LDL** and serum albumin (glycation vs. glycoxidation), (b) long-term glycated **LDL** is more readily oxidized than unglycated **LDL**, (c) oxLDL is more prone to AGE-modification, (d) AGE-modification of **LDL** strongly alters its epitope spectrum and (e) that aminoguanidine at higher concentrations (1-10 mM) inhibits copper-catalyzed **LDL** oxidation in the way of a classical antioxidant.

L16 ANSWER 11 OF 24 MEDLINE DUPLICATE 5
ACCESSION NUMBER: 97094912 MEDLINE
DOCUMENT NUMBER: 97094912
TITLE: Molecular characterization of a novel human hybrid-type receptor that binds the alpha2-macroglobulin receptor-associated protein.
AUTHOR: Jacobsen L; Madsen P; Moestrup S K; Lund A H; Tommerup N; Nykjaer A; Sottrup-Jensen L; Gliemann J; Petersen C M
CORPORATE SOURCE: Department of Medical Biochemistry, University of Aarhus, DK-8000 Aarhus C, Denmark.
SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (1996 Dec 6) 271 (49) 31379-83.
Journal code: HIV. ISSN: 0021-9258.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Cancer Journals
OTHER SOURCE: GENBANK-U60975
ENTRY MONTH: 199703
ENTRY WEEK: 19970302

AB The 39-40-kDa receptor-associated protein (RAP) binds to the members of the **low** density **lipoprotein** receptor gene family and functions as a specialized endoplasmic reticulum/Golgi chaperone. Using RAP affinity chromatography, we have purified a novel approximately 250-kDa brain protein and isolated the corresponding cDNA. The gene, designated SORL1, maps to chromosome 11q 23/24 and encodes a 2214-residue type 1 receptor containing a furin cleavage site immediately preceding the N terminus **determined** in the purified protein. The receptor, designated sorLA-1, has a short cytoplasmic tail containing a tyrosine-based internalization signal and a large external part containing (from the N-terminal): 1) a segment homologous to domains in the yeast vacuolar protein sorting 10 protein, Vps10p, that binds carboxypeptidase Y, 2) five tandemly arranged YWTD repeats and a cluster of 11 class A repeats characteristic of the **low** density **lipoprotein** receptor gene family receptors, and 3) six tandemly arranged **fibronectin** type III repeats also found in certain neural adhesion proteins. sorLA-1 may therefore be

classified as a hybrid receptor. Northern blotting revealed specific mRNA transcripts in brain, spinal cord, and testis but not in several major organs. Both RAP and an **antibody** against a synthetic peptide derived from a sequence **determined** in the mature protein **detected** sorLA-1 in crude human brain extracts. The domain structure suggests that sorLA-1 is an endocytic receptor possibly implicated in the uptake of lipoproteins and of proteases.

L16 ANSWER 12 OF 24 MEDLINE DUPLICATE 6
ACCESSION NUMBER: 96185017 MEDLINE
DOCUMENT NUMBER: 96185017
TITLE: Integrin-dependent control of inositol lipid synthesis in vascular endothelial cells and smooth muscle cells.
AUTHOR: McNamee H P; Liley H G; Ingber D E
CORPORATE SOURCE: Department of Pathology, Children's Hospital and Harvard Medical School, Boston Massachusetts 02115, USA.
CONTRACT NUMBER: HL-46491 (NHLBI)
CA35833 (NCI)
SOURCE: EXPERIMENTAL CELL RESEARCH, (1996 Apr 10) 224 (1) 116-22.
Journal code: EPB. ISSN: 0014-4827.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Cancer Journals
ENTRY MONTH: 199608
AB Extracellular matrix (ECM) molecules, such as **fibronectin** (FN), regulate fibroblast sensitivity to soluble growth factors, in part, by controlling cellular levels of phosphatidylinositol bis-phosphate (PIP2), the substrate for phospholipase C-gamma (McNamee et al., 1993, J. Cell Biol. 121, 673-678). In the present study, we extended these investigations by exploring whether cells of the vascular wall also exhibit this response and analyzing the mechanism by which adhesion to ECM regulates intracellular PIP2 mass. Capillary endothelial cells, pulmonary vascular smooth muscle cells, and C3H 101/2 fibroblasts were all found to exhibit a similar two- to threefold increase in PIP2 mass within 3 h after binding to dishes coated with FN. Furthermore, similar effects were observed using dishes coated with a variety of different ECM molecules, including collagen types I and IV as well as a synthetic RGD-containing peptide. An increase in PIP2 mass also was produced when suspended cells bound to microbeads (4.5 micron diameter; coated with RGD-peptide or anti-integrin beta 1 **antibody**) that induce local integrin clustering and focal adhesion formation, independently of cell spreading. In contrast, neither binding of soluble FN nor binding of microbeads coated with ligands for other

transmembrane surface receptors (e.g., acetylated **low** -density **lipoprotein**, **antibodies** against heparan sulfate) had any effect on PIP2 mass. While these results suggest that integrin clustering stimulates PIP2 synthesis, no change in total cellular or cytoskeletal-associated phosphatidylinositol-4-phosphate kinase (PIP kinase) activity could be **detected** when cells bound to immobilized integrin ligands. However, when focal adhesion complexes were isolated from these cells using a magnetic procedure (G. Plopper and D. E. Ingber, 1993, Biochem. Biophys. Res. Commun. 193, 571-578), this subfraction of the cytoskeleton was found to be enriched for PIP kinase activity by more than twofold relative to the whole cytoskeleton. These data suggest that ECM binding may increase PIP2 mass in vascular cells by clustering cell surface integrin receptors and activating cytoskeletal-associated PIP kinases locally within the focal adhesion complex.

L16 ANSWER 13 OF 24 SCISEARCH COPYRIGHT 2001 ISI (R)
ACCESSION NUMBER: 95:420591 SCISEARCH
THE GENUINE ARTICLE: RC789
TITLE: CHARACTERIZATION OF THE N-TERMINAL AND C-TERMINAL DOMAINS OF HUMAN **APOLIPOPROTEIN**(A) - RELEVANCE TO FIBRIN BINDING
AUTHOR: HUBY T; SCHRODER W; DOUCET C; CHAPMAN J; THILLET J (Reprint)
CORPORATE SOURCE: HOP PITIE, INSERM, U321, PAVILLON BENJAMIN DELESSERT, 83 BLVD HOP, F-75651 PARIS 13, FRANCE (Reprint); HOP PITIE, INSERM, U321, F-75651 PARIS 13, FRANCE; BAYER AG, W-5600 WUPPERTAL 1, GERMANY
COUNTRY OF AUTHOR: FRANCE; GERMANY
SOURCE: BIOCHEMISTRY, (06 JUN 1995) Vol. 34, No. 22, pp. 7385-7393.
ISSN: 0006-2960.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE
LANGUAGE: ENGLISH
REFERENCE COUNT: 32

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB The structural domains of human **apolipoprotein**(a) (**apo**(a)) in the lipoprotein(a) (Lp(a)) particle have been recently investigated by limited proteolysis [Huby, T., Doucet, C., Dieplinger, H., Chapman, J., & Thillet, J. (1994) Biochemistry 33, 3335-3341]. We have shown that **apo**(a) can be cleaved into two structural domains: one was of constant size (170 kDa) and corresponded to the C-terminal (C-ter) domain of **apo**(a). This domain was linked by a disulfide bond to **apo** B100. By contrast, the N-terminal (N-ter) domain, whose size varied according to the digested **apo**(a) isoform, was not linked to **apo** B100. We now describe the purification of these

apo(a) domains and their interaction with fibrin surfaces in an in vitro binding assay. The N-ter domain of **apo**(a) was purified as a soluble protein in a two-step procedure which involved sequential use of a heparin-Sepharose column and a lysine-Sepharose column. The C-ter domain of **apo**(a), which remained in disulfide linkage with **apo** B100 of Lp(a), was isolated as a lipoprotein particle by a combination of chromatographic steps on heparin-Sepharose and Q-Sepharose columns. This particle, termed ''mini-Lp(a)'', appeared homogeneous in nondenaturing polyacrylamide gels and exhibited a particle size (285 Angstrom) which was intermediate between that of Lp(a) (300 Angstrom) and **LDL** (265 Angstrom). The cleavage site between the respective **apo** (a) domains was **determined** by N-terminal sequencing of the purified C-ter domain. Such cleavage occurred between residues 3532 and 3533, which are located in the interkringle region between **apo**(a) kringles 4(4) and 4(5). Consequently, the C-ter domain of **apo**(a) was composed of kringles 4(5) to 4(10), kringle V, and the protease domain. The binding properties of the purified N-ter domains and mini-Lp(a) were investigated on intact and on plasmin-modified fibrin and compared to those of Lp(a). We demonstrated that the C-ter domain, in the form of mini-Lp(a), binds to fibrin in a lysine-specific manner that approached saturation, in contrast to the N-ter domains which did not bind either to fibrin or to plasmin-degraded fibrin. The apparent K-d for the mini-Lp(a) (380 +/- 30 nM) was slightly different from that of Lp(a) (150 +/- 15 nM) in binding to either plasmin-degraded or intact fibrin. This finding indicates that the C-ter domain of **apo**(a) mediates the interaction of Lp(a) with fibrin. On intact fibrin, the B-max values for Lp(a) and for mini-Lp(a) were 8.5 and 25 fmol/well, respectively; these values increased, upon plasmin digestion of fibrin, to 25 and 100 fmol/well, respectively. The increased number of accessible binding sites in the case of mini Lp(a) may result from a decreased steric hindrance as compared to Lp(a).

L16 ANSWER 14 OF 24 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.

ACCESSION NUMBER:	95162663 EMBASE
DOCUMENT NUMBER:	1995162663
TITLE:	Isolation of rat heart endothelial cells and pericytes: Evaluation of their role in the formation of extracellular matrix components.
AUTHOR:	He Q.; Spiro M.J.
CORPORATE SOURCE:	Joslin Diabetes Center, 1 Joslin Place,Boston, MA 02215, United States
SOURCE:	Journal of Molecular and Cellular Cardiology, (1995) 27/5 (1173-1183). ISSN: 0022-2828 CODEN: JMCDAY
COUNTRY:	United Kingdom
DOCUMENT TYPE:	Journal; Article
FILE SEGMENT:	018 Cardiovascular Diseases and Cardiovascular

Surgery
029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English

AB In order to facilitate investigation of the cells responsible for overproduction of type VI collagen in the extracellular matrix surrounding the capillaries of diabetic rat myocardium, procedures have been developed for the isolation from this tissue of endothelial cells as well as a cell type identified as pericytes. This was accomplished by enzymatic and mechanical disruption of ventricles from young rats (125 g) followed by removal of myocytes through their nonadherence to tissue culture surfaces. Endothelial cells were separated by fluorescence-activated cell sorting after staining with rhodamine-labeled acetylated **low** density **lipoprotein** and were identified by their monolayer growth pattern, reaction with anti-von Willebrand factor and the ability to form capillary-like tubes induced by low serum concentration. Pericytes were purified by selective scraping for removal of other cell types and were identified by their irregular shape, overlapping growth pattern at confluence, reaction with anti-smooth muscle actin and content of GLUT4 glucose transporter. Fibroblasts, visualized after staining with rhodamine-labeled .alpha.2-macroglobulin, were only rarely **detected**. Analysis of collagen by immunoblotting indicated formation by both cell types of .alpha.1(IV) collagen as well as the three subunits of type VI (.alpha.3 at 205 kDa and .alpha.1 plus .alpha.2 at 150 kDa). Both endothelial cells and pericytes demonstrated transcripts for types VI, IV and I collagen, as well as **fibronectin**, but while the level of the mRNA for type IV collagen was higher in pericytes than in endothelial cells, the reverse was true for collagens VI and I and **fibronectin**. These observations suggest that both endothelial cells and pericytes contribute to formation of the myocardial capillary matrix, but that changes involving only type VI collagen, such as occur in diabetic cardiomyopathy, may reflect a response primarily of endothelial cells.

L16 ANSWER 15 OF 24 MEDLINE DUPLICATE 7
ACCESSION NUMBER: 95123252 MEDLINE
DOCUMENT NUMBER: 95123252
TITLE: Low-density lipoprotein stimulation of mesangial cell **fibronectin** synthesis: role of protein kinase C and transforming growth factor-beta.
AUTHOR: Studer R K; Craven P A; DeRubertis F R
CORPORATE SOURCE: Veterans Affairs Medical Center, Pittsburgh, PA 15240..
SOURCE: JOURNAL OF LABORATORY AND CLINICAL MEDICINE, (1995 Jan) 125 (1) 86-95.
Journal code: IVR. ISSN: 0022-2143.
PUB. COUNTRY: United States
Searcher : Shears 308-4994

Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199504

AB **Low**-density **lipoprotein** (**LDL**) cholesterol has been implicated in the pathogenesis of glomerulosclerosis in diabetes and other forms of glomerular injury. In the present study we evaluated the effect of **LDL** on **fibronectin** synthesis in cultured rat mesangial cells (MCs) and the roles of protein kinase C (PKC) and transforming growth factor-beta (TGF-beta) in mediating this **LDL** action. In MCs, 25 micrograms to 100 micrograms/ml **LDL** increased PKC activity within 15 minutes, as reflected by enhanced in situ phosphorylation of the 80 kd myristoylated alanine-rich C kinase substrate protein, a specific endogenous substrate of PKC in MC. The same concentrations of **LDL** subsequently (18 to 72 hours) enhanced **fibronectin** synthesis, as reflected by increased incorporation of labeled methionine into **fibronectin**. GF 109203X, a selective inhibitor of PKC, blocked increases in both PKC activity and **fibronectin** synthesis induced by **LDL** in MCs. Furthermore, prior downregulation of PKC to less than 1% of basal activity by exposure of MCs to 0.5 mumol/L phorbol myristate acetate (PMA) also prevented **LDL** stimulation of **fibronectin** synthesis. The activation of PKC by **LDL** seen after 15 minutes of exposure was transient and was not observed after 4 or 48 hours of exposure of MCs to **LDL**. However, exposure to **LDL** for 48 hours, but not for 15 minutes or 4 hours, increased both maximal PKC responses to phorbol dibutyrate (PDBu) and tritiated PDBu binding to MCs by 30%. These findings suggest that chronic exposure to **LDL** increases the total PKC content in MCs and thereby might modulate responses to other PKC agonists. Neither the cyclooxygenase inhibitor piroxicam nor the thromboxane/prostaglandin endoperoxide receptor blocker Sq-29548 altered **LDL** stimulation of **fibronectin** synthesis in MCs, suggesting that this action of **LDL** was not mediated by changes in MC eicosanoid generation. By contrast, **antibody** to TGF-beta blocked **LDL** stimulation of **fibronectin** synthesis in MCs. TGF-beta bioactivity, **determined** with the mink lung epithelial cell assay, was two to three times higher in the medium of MCs cultured with **LDL** for 24 to 48 hours as compared with corresponding control values. Total TGF-beta bioactivity examined after heat activation of latent TGF-beta was also two times higher in the medium of MCs exposed to **LDL** as compared with that of controls. Prior down-regulation of PKC by exposure of MCs to PMA blocked the increases in TGF-beta bioactivity induced by **LDL**.(ABSTRACT TRUNCATED AT 400 WORDS)

L16 ANSWER 16 OF 24 MEDLINE

ACCESSION NUMBER: 94291101 MEDLINE
DOCUMENT NUMBER: 94291101
TITLE: [Imaging in atherosclerosis: scintigraphy techniques].
Imaging nell'aterosclerosi: tecniche scintigrafiche.
AUTHOR: Greco C; Scopinaro F; Centi Colella A; Campa P P
CORPORATE SOURCE: II Cattedra di Cardiologia, Universit`a degli Studi La Sapienza, Roma..
SOURCE: CARDIOLOGIA, (1993 Dec) 38 (12 Suppl 1) 13-9.
Journal code: COE. ISSN: 0393-1978.
PUB. COUNTRY: Italy
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: Italian
ENTRY MONTH: 199410

AB Noninvasive **detection** of atherosclerotic plaques remains a major challenge for clinical diagnosis, therapy and prognosis. Several approaches have been explored as a tool for thrombus imaging, using platelets, antiplatelet **antibodies** and **fibronectin** or as a direct metabolic marker as **low** density **lipoproteins** or photophrine II. We tested the affinity of a new F(ab')2 monoclonal **antibody** (TRF1) against human fragment D-dimer of cross-linked fibrin, for atherosclerotic plaques free of **detectable** thrombi on their surface. Six atherosclerotic segments of carotid and femoral arteries, and (as a control) 5 segments of atherosclerosis-free internal mammary artery, were drawn from 11 male patients undergoing bypass surgery. All segments were carefully washed in order to dissolve and remove possible endoluminal thrombi, and were subsequently cut to obtain couples of fragments of intima of similar weight, containing atherosclerotic plaques (n 16), or fatty streaks (n 12), or normal endothelium (n 20). Each fragment was separately put into a radioimmunoassay vial, and underwent a direct binding test to TRF1, or to an aspecific **antibody**, which both were labelled with 125I. The activity present in each fragment was measured with a gamma-counter after 3 h of incubation at 37 degrees C, and every hour after washing the fragments in order to remove the unbound **antibody**. No significant binding difference (expressed as per cent final activity in comparison with initial one) of the aspecific **antibody** between normal and atherosclerotic fragments was found. By contrast, TRF1 binding was significantly higher ($p < 0.001$) in atherosclerotic than in normal fragments (26.0 +/- 11.5% in atherosclerotic plaques, versus 9.23 +/- 9% in fatty streaks, versus 1.9 +/- 0.6% in normal endothelium.(ABSTRACT TRUNCATED AT 250 WORDS)

L16 ANSWER 17 OF 24 MEDLINE DUPLICATE 8
ACCESSION NUMBER: 93135439 MEDLINE
DOCUMENT NUMBER: 93135439
TITLE: Cell-matrix interactions in the genesis of

arteriosclerosis and atheroma. Effect of aging.

AUTHOR: Robert L; Jacob M P; Labat-Robert J
CORPORATE SOURCE: Laboratoire de Biologie du Tissu Conjonctif, URA CNRS 1460, Faculte de Medecine, Universite Paris XII, Creteil, France..

SOURCE: ANNALS OF THE NEW YORK ACADEMY OF SCIENCES, (1992 Dec 26) 673 331-41. Ref: 41
Journal code: 5NM. ISSN: 0077-8923.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Cancer Journals
ENTRY MONTH: 199304

AB The progression of atheroarteriosclerosis was shown to be age dependent. This designation covers two separate entities: **arteriosclerosis**, the progressive and diffuse hardening of the walls of arteries with loss of elasticity, and atheromatous plaque formation, which can start early in life according to nutrition and genetic factors (**LDL**-receptor expression). Lipoprotein-receptor interactions play a crucial role in lipidic plaque formation. There is, however, no indication that the diffuse hardening of the vascular wall would also be influenced by these mechanisms. We described recently a high-affinity receptor for elastin peptides, present on smooth muscle cells, fibroblasts, and also on monocytes and PMNs. When activated, this receptor will increase intracellular calcium. Circulating elastin peptides were **determined** by a sensitive Elisa method and found to be between 0.1 and 20 micrograms/ml, in the range of activation of the elastin receptor. They increase in obliterative arteriopathies and type IIb hyperlipidemia. Elastolysis accompanies aging and vascular pathology; the sensitivity of this receptor changes with age, intracellular Ca++ increases, but the receptor appears to be uncoupled from its normal transmission mechanism. These results may well explain the increasing diffuse calcification of the vessel wall. The previously demonstrated potentiation of cholesterol deposition in elastic fibers by calcium is in agreement with simultaneous deposition of calcium and lipids. The recent demonstration of the efficient competition of **fibronectin** for **LDL** in proteoglycan-**LDL** complexes suggests that this reaction may be involved in foam cell formation by the opsonization of **LDL** for phagocytosis. **Fibronectin** was shown to accumulate in atherosclerotic plaques. Altogether these recent results confirm the importance of cell-matrix interactions in atherogenesis and lead to a better understanding of the age dependence of these disease processes.

L16 ANSWER 18 OF 24 SCISEARCH COPYRIGHT 2001 ISI (R)
ACCESSION NUMBER: 92:231264 SCISEARCH
THE GENUINE ARTICLE: HM079
TITLE: PATHOPHYSIOLOGY OF ELEVATED ASCITES-FLUID CHOLESTEROL IN MALIGNANT ASCITES - INCREASED ASCITES TO SERUM RELATION OF PROTEINS AND LIPOPROTEINS IN PATIENTS WITH PERITONEAL CARCINOMATOSIS AS COMPARED TO PATIENTS WITH CIRRHOSIS OF THE LIVER
AUTHOR: JUNGST D (Reprint); XIE Y N; GERBES A L
CORPORATE SOURCE: UNIV MUNICH, KLINIKUM GROSSHADERN, DEPT MED 2, MARCHIONINISTR 15, W-8000 MUNICH 70, GERMANY (Reprint)
COUNTRY OF AUTHOR: GERMANY
SOURCE: JOURNAL OF HEPATOLOGY, (MAR 1992) Vol. 14, No. 2-3, pp. 244-248.
ISSN: 0168-8278.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE; CLIN
LANGUAGE: ENGLISH
REFERENCE COUNT: 25
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB The existence of marked elevations of ascitic fluid cholesterol has been observed in patients with peritoneal carcinomatosis compared to patients with cirrhosis and has been found useful in differential diagnosis. This finding could be caused by an enhanced movement of plasma lipoproteins into the peritoneal cavity. To test this hypothesis we **determined** the fasting concentrations of total, high density lipoprotein (HDL)- and **low** density **lipoprotein** (**LDL**)-cholesterol, **apolipoprotein**-A1 (**apo**-A1) and **apolipoprotein**-B (**apo**-B) in serum and ascites of 17 patients with cirrhosis and 16 patients with peritoneal carcinomatosis. The movement of proteins from plasma to ascites was calculated from the ascites/serum concentration ratios of six different sized proteins with a molecular mass ranging from 54 kDa to 971 kDa. Mean values (mg/dl) for total cholesterol (92.6 vs. 21.0), HDL-cholesterol (15.6 vs. 1.8), **LDL**-cholesterol (63.4 vs. 16.1), **apo**-A1 (50.2 vs. 13.6) and **apo**-B (41.2 vs. 12.9) in ascites were significantly higher in peritoneal carcinomatosis than in cirrhosis. These differences could only partially be explained by the higher serum concentrations of these parameters in peritoneal carcinomatosis, but were mainly due to a lower selectivity for the movement of plasma proteins and lipoproteins into ascites (mean ascites/serum (A/S) ratio: 0.30-0.77) in peritoneal carcinomatosis as compared to cirrhosis (mean ascites/serum ratio: 0.11-0.21). In both groups about 85% of the total cholesterol in serum and ascites consisted of HDL- and **LDL**-cholesterol. These findings support the hypothesis that elevations in ascitic cholesterol in peritoneal carcinomatosis

compared to cirrhosis are mainly caused by the increased movement of plasma HDL and **LDL** into the peritoneal cavity.

L16 ANSWER 19 OF 24 MEDLINE DUPLICATE 9
ACCESSION NUMBER: 93103360 MEDLINE
DOCUMENT NUMBER: 93103360
TITLE: Cytokine regulation of macrophage **apo** E secretion: opposing effects of GM-CSF and TGF-beta.
AUTHOR: Zuckerman S H; Evans G F; O'Neal L
CORPORATE SOURCE: Lilly Research Labs, Indianapolis, IN 46285.
SOURCE: ATHEROSCLEROSIS, (1992 Oct) 96 (2-3) 203-14.
Journal code: 95X. ISSN: 0021-9150.
PUB. COUNTRY: Netherlands
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199303

AB Biosynthesis of **apolipoprotein** (**apo**) E has been previously demonstrated to be regulated in macrophages by intracellular free cholesterol levels as well as by macrophage activating factors. In this report, the regulation of **apo** E secretion by cytokines **detected** within atherosclerotic lesions has been investigated. Granulocyte macrophage-colony stimulating factor (GM-CSF) stimulated macrophages had a 3-5-fold reduction in **apo** E secretion, comparable to that observed for gamma interferon (IFN gamma), while tumor necrosis factor alpha (TNF alpha) and interleukin 1 beta (IL-1 beta) resulted in a 2-fold decrease. In contrast to the reduction in **apo** E secretion by these cytokines, transforming growth factor beta (TGF-beta) stimulated macrophages secreted 3-fold greater amounts of **apo** E than controls. The reduced secretion of **apo** E by GM-CSF was reversible, heat labile, dose dependent, maximal 48 h after cytokine exposure and was coincident with an increase in **fibronectin** secretion. The opposing effects of GM-CSF and TGF-beta on **apo** E secretion were consistent with similar changes **detected** in **apo** E mRNA levels. Cytokine effects on **apo** E secretion in cholesterol loaded macrophages were also investigated and found to be similar to the non-loaded cells with GM-CSF decreasing and TGF-beta increasing **apo** E secretion. The observed differences in **apo** E secretion did not correlate with any significant changes in either cellular cholesterol distribution in the non-cholesterol loaded macrophages or in basal ACAT activity. In addition to changes in **apo** E secretion, cytokine treated macrophages pulsed with [14C]oleate and acetylated **LDL** for 2-6 h had a 2-fold increase (GM-CSF) or decrease (TGF-beta) in cholesterol esterification. Therefore, GM-CSF and TGF-beta mediated changes in **apo** E secretion may occur through a mechanism independent of changes in cellular free cholesterol levels. These results suggest

that cytokines expressed within an atheroma may play an important role in the modulation of macrophage mediated reverse cholesterol transport.

L16 ANSWER 20 OF 24 JICST-EPlus COPYRIGHT 2001 JST
ACCESSION NUMBER: 920012448 JICST-EPlus
TITLE: The Role of Extracellular Components on the Development of Atherosclerosis.
AUTHOR: SAKATA NORIYUKI; JIMI SHIRO; TAKEBAYASHI SHIGEO
CORPORATE SOURCE: Fukuoka Univ., School of Medicine
SOURCE: Domyaku Koka (Journal of Japan Atherosclerosis Society), (1991) vol. 19, no. 9/10, pp. 795-803. Journal Code: Y0035A (Fig. 14, Tbl. 1, Ref. 15) ISSN: 0386-2682
PUB. COUNTRY: Japan
DOCUMENT TYPE: Journal; Article
LANGUAGE: Japanese
STATUS: New
AB The relation between extracellular matrices and smooth muscle cells has be recognized as important for the development and regression of atherosclerotic lesions. We attempted to clarify the role of extracellular components on atherogenesis. Cellular intima have already been **detected** on both lateral walls and apexes of coronary arterial bifurcations. On the lateral wall, the intima was thickened with age, and there was an increase in the volume fraction of the extracellular components, as well as an accumulation of lipids after 40 years of age. The histochemical examination demonstrated that **LDL** and lipid particles had deposited in the area of the thickened intima where type I or V collagen was distributed. Type V collagen more strongly repressed this attachment, spreading and proliferation of the cultured smooth muscle cells that did the **fibronectin**, or types I, III, and IV collagen. However, the collagen synthesis of cultured smooth muscle cells was enhanced by type V collagen. Furthermore, **LDL** and Cu-oxidized **LDL** promoted the collagen synthesis of cultured smooth muscle cells approximately six and twenty-three times, respectively, as much as the controls. These results suggest that extracellular components in the intima including type V collagen, **LDL** and oxidized **LDL** play an important role in atherogenesis. (author abst.)

L16 ANSWER 21 OF 24 MEDLINE
ACCESSION NUMBER: 90197518 MEDLINE
DOCUMENT NUMBER: 90197518
TITLE: Fate of fibrinogen in human arterial intima.
AUTHOR: Smith E B; Keen G A; Grant A; Stirk C
CORPORATE SOURCE: University of Aberdeen, Department of Clinical Biochemistry, Foresterhill, Scotland..
SOURCE: ARTERIOSCLEROSIS, (1990 Mar-Apr) 10 (2) 263-75.
Searcher : Shears 308-4994

Journal code: 89S. ISSN: 0276-5047.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199006
AB Fibrinogen and fibrinogen/fibrin-related antigen (total FRA) was measured in human normal intima and different types of atherosclerotic lesions and mural thrombi. The amount showed marked variation between groups of tissue samples, but within each group there was a significant correlation between levels of total FRA and **low** density **lipoprotein** (**LDL**), suggesting that some common factor must influence their influx or retention. The total FRA were analyzed by gradient sodium dodecyl sulfate polyacrylamide gel electrophoresis and immunoblotting with antisera to whole fibrinogen and fragments D and E, and fibrinopeptide A (FPA). All intimal samples (but not thrombi) contained fragment X, the first product of plasmin digestion of fibrinogen, but fragment Y was present in only half the samples, and no core-fragment E containing FPA was **detected** in any sample, suggesting that fibrinogenolysis is limited. By contrast, all samples contained fragment E, which was negative for FPA, so presumably derived from fibrin; they also contained fragments D-dimer and DY, which are characteristic degradation products of cross-linked fibrin. There were no differences between samples obtained during reconstructive vascular surgery and samples obtained at autopsy, so the patterns appear to represent the steady state. This implies that within the intima there is continuous formation of cross-linked fibrin and continuous fibrinolysis, both processes generating fragments that may have atherogenic properties.

L16 ANSWER 22 OF 24 MEDLINE DUPLICATE 10
ACCESSION NUMBER: 87122267 MEDLINE
DOCUMENT NUMBER: 87122267
TITLE: [Effect of the modification of low density lipoproteins by thrombin on their interaction with **fibronectin**].
Vliianie modifikatsii lipoproteidov nizkoi plotnosti trombinom na ikh vzaimodeistvie s fibronektinom.
AUTHOR: Chulkova T M
SOURCE: VOPROSY MEDITSINSKOI KHIMII, (1986 Nov-Dec) 32 (6) 70-3.
Journal code: XIQ. ISSN: 0042-8809.
PUB. COUNTRY: USSR
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: Russian
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198705
AB Interaction of native and thrombin-modified human **low**

density **lipoproteins** (**LDL**) with immobilized homologous **fibronectin** (either covalently bound to Sepharose or adsorbed from blood serum on collagen-Sepharose) was studied. Treatment of **LDL** with thrombin at pH 7.5 and 37 degrees within 60 min (thrombin/**apo** B ratio 1:20 w/w) led to formation in **LDL** preparations of 3 new fragments of apoprotein B which were **detected** by polyacrylamide gel electrophoresis in presence of sodium dodecylsulfate. Chromatography of native and thrombinmodified **LDL** on **fibronectin** -Sepharose showed that 30% of the modified **LDL** and 2% of native **LDL** were bound to **fibronectin**-Sepharose at physiological pH values and NaCl concentrations. Study of the interaction of **LDL** with **fibronectin** adsorbed on collagen-Sepharose showed that thrombin-treated **LDL** partially released **fibronectin** from the sorbent due to the formation of a modified **LDL-fibronectin** complex. Native **LDL** did not act in a similar manner. Complexes of modified, **LDL** with **fibronectin** were **detected** under conditions of both electrophoresis in 3% polyacrylamide gel and immunoelectrophoresis. Interaction of **LDL** with **fibronectin** may promote accumulation of lipoproteins in the vascular wall and thus may serve as a model system for evaluation of the extent of atherogeneity of **LDL** and **detection** of the modified **LDL** in vivo.

L16 ANSWER 23 OF 24 BIOSIS COPYRIGHT 2001 BIOSIS DUPLICATE 11
ACCESSION NUMBER: 1984:323400 BIOSIS
DOCUMENT NUMBER: BA78:59880
TITLE: LIPO PROTEINS CONTAINING **APO** PROTEIN B ARE A MAJOR REGULATOR OF NEUTROPHIL RESPONSES TO MONO SODIUM URATE CRYSTALS.
AUTHOR(S): TERKELTAUB R; CURTISS L K; TENNER A J; GINSBERG M H
CORPORATE SOURCE: DEP. IMMUNOLOGY, DIV. RHEUMATOLOGY, SCRIPPS CLINIC RES. FOUNDATION, LA JOLLA, CA 92037.
SOURCE: J CLIN INVEST, (1984) 73 (6), 1719-1730.
CODEN: JCINAO. ISSN: 0021-9738.
FILE SEGMENT: BA; OLD
LANGUAGE: English
AB The inflammatory response to intraarticular urate crystals is variable in gouty arthritis. One source of variability may be the modulation of cellular responses by crystal-bound proteins. Three **apolipoproteins** were identified among the polypeptides bound to urate crystals exposed to [human] plasma. The **apolipoproteins** wree immunochemically identified as apoprotein A-I, apoprotein B (**apo** B) and apoprotein E. Because neutrophils play a central role in acute gout, the potential effects of lipoproteins on neutrophil-urate crystal interactions were studied. Plasma profoundly inhibited urate crystal-induced neutrophil luminol-dependent chemiluminescence (CL). Lipoprotein

depletion completely abrogated the inhibitory effect of plasma on urate-induced CL. The inhibitory activity of lipoprotein-depleted plasma was restored by adding back the d .ltoreq. 1.25 g/cm3 lipoprotein fraction. Plasma also inhibited urate crystal-induced neutrophil superoxide generation and cytolysis (lactic dehydrogenase loss). This inhibition was significantly diminshed by lipoprotein depletion, indicating that the lipoprotein effect was not limited to CL. **Apo** B lipoproteins were shown to be the inhibitory species in plasma. Binding of **apo** B lipoproteins to urate crystals and inhibition of CL was also seen in the absence of other plasma proteins. The binding of whole lipoprotein particles to the crystals was verified by **detection** of crystal-associated cholesterol in addition to the apoprotein. The effects of **LDL** on urate crystal-induced CL were stimulus specific. The effects of depletion of **apo** B lipoproteins on plasma suppression of urate crystal-induced CL appeared to be unique. Plasmas or sera depleted of other urate crystal-binding proteins including fibrinogen, **fibronectin**, C1q, and IgG retained virtually all their CL inhibitory activity. Lipoproteins containing **apo** B are thus a major regulator of neutrophil responses to urate crystals. These lipoproteins are present in variable concentration in synovial fluid and may exert an important influence on the course of gout.

L16 ANSWER 24 OF 24 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.

ACCESSION NUMBER:	84164384 EMBASE
DOCUMENT NUMBER:	1984164384
TITLE:	Acute phase proteins with special reference to C-reactive protein and related proteins (pentaxins) and serum amyloid A protein.
AUTHOR:	Pepys M.B.; Baltz M.L.
CORPORATE SOURCE:	Immunological Medicine Unit, Department of Medicine, Royal Postgraduate Medical School, Hammersmith Hospital, London, United Kingdom
SOURCE:	Advances in Immunology, (1983) VOL. 34/- (141-212). CODEN: ADIMAV
COUNTRY:	United States
DOCUMENT TYPE:	Journal
FILE SEGMENT:	006 Internal Medicine 029 Clinical Biochemistry 026 Immunology, Serology and Transplantation 005 General Pathology and Pathological Anatomy 015 Chest Diseases, Thoracic Surgery and Tuberculosis
LANGUAGE:	English

AB The acute phase response among plasma proteins is a normal response to tissue injury and is therefore a fundamental aspect of many diverse disease processes. It probably usually has a beneficial net function in limiting damage and promoting repair but in some

circumstances it may have pathological consequences. Sustained high levels of acute phase proteins and especially SAA are associated with the development of amyloidosis in some individuals. Increased concentrations of CRP may, by activating the complement system, contribute to inflammation and enhance tissue damage. Failure of the normal or appropriate CRP response may also possibly have deleterious effects. SAA is a polymorphic protein which is normally present only in trace amounts but which, during the acute phase response, becomes one of the major **apolipoproteins** associated with high-density lipoprotein particles. The function of apoSAA is not known but it must have considerable physiological significance apart from its role as the putative precursor of amyloid A protein fibrils. CRP and SAP have been very stably conserved throughout vertebrate evolution and homologous proteins are apparently present even in vertebrates. This strongly suggests that they have important functions although these have not yet been precisely delineated. The main role of CRP may be to provide for enhanced clearance of inappropriate materials from the plasma whether these are of extrinsic origin, such as microorganisms and their products, or the autologous products of cell damage and death. The interaction between aggregated CRP and plasma **low** -density **lipoprotein** may play a significant part in the normal function of CRP and may also have a role in lipoprotein metabolism, clearance, and deposition. SAP is a normal tissue protein as well as being a plasma protein. Aggregated SAP selectively binds **fibronectin** and this may represent an aspect of the normal function of SAP. The deposition of SAP in amyloid is evidently not a normal function but it is not known whether this deposition is involved in the pathogenesis of amyloid or whether it is merely an epiphenomenon. In any case immunohistochemical staining for SAP is useful in the diagnosis of amyloid, in investigation of glomerulonephritis, and in studying disorders of elastic tissue. Regardless of its physiological or pathophysiological functions, the assay of serum CRP is a valuable aid to clinical management in a number of different situations and in different diseases provided results are interpreted in the light of full clinical information. It is a sensitive **screening** test for organic disease, it is useful for monitoring the activity of those infective, inflammatory, and neoplastic diseases which provoke major elevations, it is a sensitive test for **detection** of intercurrent or persistent infection, and it helps in monitoring resolution after acute events such as major surgery or myocardial infarction.

(FILE 'MEDLINE' ENTERED AT 12:28:43 ON 16 MAR 2001)

L17	14565	SEA	FILE=MEDLINE	ABB=ON	PLU=ON	"LIPOPROTEINS, LDL"/CT
L18	12043	SEA	FILE=MEDLINE	ABB=ON	PLU=ON	FIBRONECTINS/CT
L19	43	SEA	FILE=MEDLINE	ABB=ON	PLU=ON	L17 AND L18
L20	55525	SEA	FILE=MEDLINE	ABB=ON	PLU=ON	ANTIBODIES/CT

Searcher : Shears 308-4994

```
L21           3 SEA FILE=MEDLINE ABB=ON  PLU=ON  L19 AND L20


L17       14565 SEA FILE=MEDLINE ABB=ON  PLU=ON  "LIPOPROTEINS, LDL"/CT
L18       12043 SEA FILE=MEDLINE ABB=ON  PLU=ON  FIBRONECTINS/CT
L19          43 SEA FILE=MEDLINE ABB=ON  PLU=ON  L17 AND L18
L22       37871 SEA FILE=MEDLINE ABB=ON  PLU=ON  ARTERIOSCLEROSIS/CT
L23           7 SEA FILE=MEDLINE ABB=ON  PLU=ON  L19 AND L22


L17       14565 SEA FILE=MEDLINE ABB=ON  PLU=ON  "LIPOPROTEINS, LDL"/CT
L20       55525 SEA FILE=MEDLINE ABB=ON  PLU=ON  ANTIBODIES/CT
L26        5647 SEA FILE=MEDLINE ABB=ON  PLU=ON  APOLIPOPROTEINS/CT
L27         902 SEA FILE=MEDLINE ABB=ON  PLU=ON  L17 AND L26
L28           4 SEA FILE=MEDLINE ABB=ON  PLU=ON  L27 AND L20


L29          14 L21 OR L23 OR L28

=> d 1-14 .beverlymed

L29  ANSWER 1 OF 14  MEDLINE
AN   1998328408     MEDLINE
TI   Expression and localization of matrix metalloproteinase-12 in the
     aorta of cholesterol-fed rabbits: relationship to lesion
     development.
AU   Matsumoto S; Kobayashi T; Katoh M; Saito S; Ikeda Y; Kobori M;
     Masuho Y; Watanabe T
SO   AMERICAN JOURNAL OF PATHOLOGY, (1998 Jul) 153 (1) 109-19.
     Journal code: 3RS. ISSN: 0002-9440.
AB   Degradation of extracellular matrix (ECM) proteins in the aorta is a
     critical step for the development of atherosclerosis. Expression of
     matrix metalloproteinase (MMP)-12 (macrophage elastase), an
     elastin-degrading proteinase in the MMP family, was investigated in
     the thoracic aorta of rabbits fed a 1% cholesterol-containing diet
     for 16 weeks. In the atherosclerotic lesions, MMP-12 was produced
     abundantly at both the mRNA and protein levels, whereas no
     expression was observed in the normal rabbit aortas. The principal
     source of MMP-12 was macrophage foam cells (MFCs) that had
     infiltrated the atherosclerotic intima; this was demonstrated in
     both in vitro culture studies of MFCs purified from atherosclerotic
     lesions and immunohistochemical studies of aortic lesions.
     Additional biochemical studies using recombinant rabbit MMP-12
     revealed that MMP-12 digested elastin, type IV collagen, and
     fibronectin and also activated MMP-2 and MMP-3. Expression of MMP-12
     by human macrophage cell lines was increased by stimulation with
     acetylated low-density lipoprotein, implying augmentation of MMP-12
     production during foam cell formation. Increased expression of
     MMP-12 in atherosclerotic lesions, concomitant with foam cell
```

generation, which triggers the acceleration of ECM breakdown, is likely to be a critical step in the initiation and progression of the atherosclerotic cascade.

L29 ANSWER 2 OF 14 MEDLINE
AN 1998073713 MEDLINE
TI In vitro interactions of oxidatively modified LDL with type I, II, III, IV, and V collagen, laminin, fibronectin, and poly-D-lysine [published erratum appears in Arterioscler Thromb Vasc Biol 1998 Jul;18(7):1197].
AU Greilberger J; Schmut O; Jurgens G
SO ARTERIOSCLEROSIS, THROMBOSIS, AND VASCULAR BIOLOGY, (1997 Nov) 17 (11) 2721-8.
Journal code: B89. ISSN: 1079-5642.
AB The accumulation of LDL in the arterial intima is considered a key event in atherogenesis. We investigated the binding of oxidized LDL (ox-LDL) to microtiter plates coated with type I or II collagen, laminin, fibronectin, or poly-D-lysine. Oxidation of LDL, 125I-LDL, or Eu(3+)-LDL was performed with CuCl2, varying the time of oxidation. Bound lipoprotein was assessed by counting radioactivity or fluorescence in the wells. Binding of highly ox-LDL in PBS followed the order: type I collagen > poly-D-lysine > type II collagen > laminin > fibronectin. Comparing various collagen types, the binding of ox-LDL followed the order: type I > type V and, type III > type IV > type II collagen. Binding of ox-LDL in PBS was dependent on an increase in negative charge of ox-LDL. Testing certain amino acids as competitors for binding of highly ox-LDL to type I collagen put lysine first, followed by arginine and histidine. On laminin, histidine competed most, followed by lysine and arginine. When studying the influence of Na+, K+, Ca2+, Mg2+ (equivalent to their concentrations in the interstitial fluid), native LDL, moderately ox-LDL, and highly ox-LDL showed the same affinity to type I collagen. However, a fivefold dilution of the buffer increased the affinity of moderately and highly ox-LDL 3.9- and 10-fold compared with native LDL. Application of the F(ab')2 from a monoclonal antibody to ox-LDL revealed a strong competition of the binding of highly ox-LDL to type II collagen (60%), laminin (35%), type I collagen (20%), and poly-D-lysine (15%), whereas the binding to fibronectin was not affected.

L29 ANSWER 3 OF 14 MEDLINE
AN 97396073 MEDLINE
TI Characterization of a specific polyclonal antibody against 13-hydroperoxyoctadecadienoic acid-modified protein: formation of lipid hydroperoxide-modified apoB-100 in oxidized LDL.
AU Kato Y; Makino Y; Osawa T
SO JOURNAL OF LIPID RESEARCH, (1997 Jul) 38 (7) 1334-46.
Journal code: IX3. ISSN: 0022-2275.
AB Lipid hydroperoxide may react with protein or amino phospholipid

without secondary decomposition. We prepared a polyclonal antibody to lipid hydroperoxide-modified proteins using 13S-hydroperoxy-9Z, 11E-octadecadienoic acid-modified keyhole limpet hemocyanin (13-HPODE-KLH) as immunogen. The antibody recognized 13-HPODE-modified bovine serum albumin (BSA), but not aldehyde-modified proteins, such as malondialdehyde-modified BSA. The antibody also recognized adducts derived from 13-HPODE and 13S-hydroperoxy-9Z, 11E, 15Z-octadecatrienoic acid (13-HPOTRE(alpha)). The oxidized alpha-linolenic acid- and linoleate-protein adducts were recognized by the antibody. Oxidized phospholipid-protein adducts were scarcely recognized by the antibody. However, when ester bonds of phospholipids containing linoleic acid were hydrolyzed by alkaline treatment, the cross-reactivities appeared. The result suggests that a phospholipid hydroperoxide can react with a protein directly or indirectly, and a carboxyl terminal (COOH) of the lipid in an adduct was needed as an epitope. Oxidized LDL (ox-LDL) was prepared by the incubation of LDL with copper ion or 2,2'-azobis(2-amidinopropane)dihydrochloride (AAPH), and the formation of lipid hydroperoxide-modified apolipoprotein was confirmed using the antibody. A slight immunoreactivity was observed in ox-LDL without alkaline treatment. When the ox-LDL was treated with alkali to hydrolyze the ester bonds of the lipid, enhanced antigenicity appeared with time-dependency. The results suggest that lipid hydroperoxide-modified apolipoprotein was formed during the oxidation of LDL.

L29 ANSWER 4 OF 14 MEDLINE
AN 97112458 MEDLINE
TI Inhibition of cholesteryl ester transfer protein by apolipoproteins, lipopolysaccharides, and cholesteryl sulfate.
AU Connolly D T; Krul E S; Heuvelman D; Glenn K C
SO BIOCHIMICA ET BIOPHYSICA ACTA, (1996 Nov 22) 1304 (2) 145-60. Journal code: A0W. ISSN: 0006-3002.
AB Cholesteryl ester transfer protein (CETP) mediates the exchange of cholesteryl esters and triglycerides between lipoproteins in the plasma. In studies dealing with the mechanism of CETP-mediated lipid transfer, we have examined the effects of several classes of biomolecules, including apolipoproteins and related synthetic peptides, cholesteryl sulfate, and lipopolysaccharides. In all cases, the molecules were inhibitory and their effects were associated with modifications of either HDL, LDL, or both. However, the probable mechanisms were distinct for each class of inhibitor. Inhibition of lipid transfer activity by apolipoprotein A-I was correlated with an increase in the apolipoprotein A-I content of HDL but not LDL, whereas the primary effect of cholesteryl sulfate was associated with modification of LDL, and only modest alteration of HDL. Lipopolysaccharides were found to modify the size and charge properties of both LDL and HDL over the same concentration ranges that affected CETP activity, but might also interact directly with

CETP. It is suggested from the present studies that a variety of biomolecules that can interact with lipoproteins under natural or pathological situations have the potential to modify CETP activity, which in turn could affect normal lipoprotein composition and distribution.

L29 ANSWER 5 OF 14 MEDLINE
AN 95084362 MEDLINE
TI Plasma fibronectin and estrogen replacement therapy.
AU Saleh A A; Dorey L G; Dombrowski M P; Hirata J; Mammen E F
SO THROMBOSIS RESEARCH, (1994 Aug 1) 75 (3) 319-22.
Journal code: VRN. ISSN: 0049-3848.

L29 ANSWER 6 OF 14 MEDLINE
AN 95032306 MEDLINE
TI Atherogenic levels of low density lipoprotein alter the permeability and composition of the endothelial barrier.
AU Guretzki H J; Gerbitz K D; Olgemoller B; Schleicher E
SO ATHEROSCLEROSIS, (1994 May) 107 (1) 15-24.
Journal code: 95X. ISSN: 0021-9150.
AB In the present study we investigated the influence of elevated low density lipoprotein (LDL) concentration on endothelial permeability. Endothelial cells were cultured on microporous membranes until confluence and albumin, dextran and LDL transfer across endothelial monolayers was determined to assess macromolecular permeability. Exposure of proliferating aortic endothelial cells to LDL levels of more than 1 mg/ml LDL-cholesterol induced a concentration-dependent exponential increase in the permeability of confluent endothelial monolayers. Acute addition of high LDL concentration did not alter macromolecular permeability. Once elevated permeability was induced, it persisted. It was not readily reversible after addition of normal LDL levels. Change in permeability was accompanied by a selective decrease in basement membrane associated heparan sulfate proteoglycan (HSPG) content. The apparent parallel between the loss in endothelial barrier function and HSPG decrease implicates a connection between the two events. Prolonged, but not acute, incubation with antiserum directed against the core-protein of HSPG also led to increased permeability, suggesting a causal role of HSPG for the proper function of endothelium. The fact that non-atherogenic LDL-cholesterol levels had no effect indicates that a 'threshold' concentration for LDL-cholesterol may exist, leading to nondenuding injury in the endothelial barrier as an early event in development of atherosclerosis.

L29 ANSWER 7 OF 14 MEDLINE
AN 93002913 MEDLINE
TI Lipoproteins enhance fibronectin binding to adherent cells.
AU Checovich W J; Schultz R L; Mosher D F
SO ARTERIOSCLEROSIS AND THROMBOSIS, (1992 Oct) 12 (10) 1122-30.

Journal code: AZ1. ISSN: 1049-8834.

AB We have identified very low density (VLDL) and low density (LDL) lipoproteins as blood plasma components that enhance the binding and deposition of fibronectin into the extracellular matrices of cultured MG-63 osteosarcoma cells and human fibroblasts. The lipoproteins increased the binding and deposition of iodinated fibronectin by MG-63 cells threefold over control levels. LDL also increased the deposition of multimeric fibronectin into extracellular matrix as assessed by gel electrophoresis and fluorescence microscopy. High density lipoprotein (HDL) and the d > 1.21 g/ml nonlipoprotein fraction had less activity. Enhancement of binding of fibronectin was observed within 15 minutes, when binding was largely reversible. LDL also increased the binding of a fragment containing the 70-kd amino-terminal region of fibronectin that is primarily responsible for the reversible binding of fibronectin to cell layers. LDL had to be present simultaneously with radiolabeled fibronectin to exert an effect on fibronectin binding. LDL enhanced fibronectin binding equally well to normal skin fibroblasts and to familial hypercholesterolemic fibroblasts lacking the LDL receptor. Acetylation of LDL, performed to block its interaction with the LDL receptor, did not diminish the enhancement of fibronectin binding to MG-63 cells. These results indicate that LDL and VLDL interact with fibronectin to potentiate binding to monolayer cells through a pathway that does not involve the LDL receptor.

L29 ANSWER 8 OF 14 MEDLINE

AN 92011281 MEDLINE

TI Extracellular matrix permits the expression of von Willebrand's factor, uptake of di-I-acetylated low density lipoprotein and secretion of prostacyclin in cultures of endothelial cells from rat brain microvessels.

AU Doron D A; Jacobowitz D M; Heldman E; Feuerstein G; Pollard H B; Hallenbeck J M

SO IN VITRO CELLULAR AND DEVELOPMENTAL BIOLOGY, (1991 Sep) 27A (9) 689-97.
Journal code: HEQ. ISSN: 0883-8364.

AB Microvascular endothelial cells from the adult rat brain were cultured on Matrigel and found to express many differentiated properties including secretion of prostacyclin (PGI2) and von Willebrand's factor (vWF). Brain microvascular endothelial cells (BMECs) were purified by dextran and percoll gradients after enzymatic treatment and cultured under various conditions. BMECs that were plated on Matrigel stained positively for factor VIII-related antigen and incorporated Di-I-acetylated low density lipoprotein, whereas BMEC plated on fibronectin, gelatin, or uncoated dishes did not express any of the above properties which are characteristic of endothelial cells. vWF was measured by a sensitive ELISA in the culture media of BMECs plated on different types of matrices. Specificity of the anti-human vWF antibodies for

the rat vWF was verified by immunoabsorption on a solid phase, sodium dodecyl sulfate, and Western blot analysis. BMECs also secreted vWF into the culture media only when the cells were plated on Matrigel, and this secretion was augmented after a 6 h incubation with an interleukin-1 tumor necrosis factor-alpha mixture, but not by lipopolysaccharide. From different matrices tested, only Matrigel permitted the secretion of PGI2 by BMECs. Cells also proved to be sensitive to mechanical stimulation and became refractory to secretagogue if the mechanical stimulation was serially repeated. Under the best conditions, stimulation of the cells with bradykinin (1 microM) substantially increased PGI2 secretion. These data indicate that growth of BMECs on Matrigel in vitro permits the expression of classical endothelial cell markers in a manner similar to the behavior of these cells in situ.

L29 ANSWER 9 OF 14 MEDLINE
AN 90197518 MEDLINE
TI Fate of fibrinogen in human arterial intima.
AU Smith E B; Keen G A; Grant A; Stirk C
SO ARTERIOSCLEROSIS, (1990 Mar-Apr) 10 (2) 263-75.
Journal code: 89S. ISSN: 0276-5047.
AB Fibrinogen and fibrinogen/fibrin-related antigen (total FRA) was measured in human normal intima and different types of atherosclerotic lesions and mural thrombi. The amount showed marked variation between groups of tissue samples, but within each group there was a significant correlation between levels of total FRA and low density lipoprotein (LDL), suggesting that some common factor must influence their influx or retention. The total FRA were analyzed by gradient sodium dodecyl sulfate polyacrylamide gel electrophoresis and immunoblotting with antisera to whole fibrinogen and fragments D and E, and fibrinopeptide A (FPA). All intimal samples (but not thrombi) contained fragment X, the first product of plasmin digestion of fibrinogen, but fragment Y was present in only half the samples, and no core-fragment E containing FPA was detected in any sample, suggesting that fibrinogenolysis is limited. By contrast, all samples contained fragment E, which was negative for FPA, so presumably derived from fibrin; they also contained fragments D-dimer and DY, which are characteristic degradation products of cross-linked fibrin. There were no differences between samples obtained during reconstructive vascular surgery and samples obtained at autopsy, so the patterns appear to represent the steady state. This implies that within the intima there is continuous formation of cross-linked fibrin and continuous fibrinolysis, both processes generating fragments that may have atherogenic properties.

L29 ANSWER 10 OF 14 MEDLINE
AN 87184651 MEDLINE
TI On the possibility of the unification of drug targeting systems. Studies with liposome transport to the mixtures of target antigens.

AU Trubetskoy V S; Berdichevsky V R; Efremov E E; Torchilin V P
SO BIOCHEMICAL PHARMACOLOGY, (1987 Mar 15) 36 (6) 839-42.
Journal code: 9Z4. ISSN: 0006-2952.
AB In order to make the drug targeting system more effective, simple and technological, we suggest creation of drug-bearing conjugates capable of simultaneous binding with different antigenic components of the target via specific antibodies. It is supposed that the targeted therapy should include sequential administration of the mixture of modified antibodies (or other specific vectors) against different components of affected tissue and, upon antibody accumulation in the desired region, administration of modified drugs or drug carrying systems which can recognize and bind with the target via accumulated antibodies due to the interaction between vector modifier and carrier modifier. Using as a model system monolayers consisting of the mixture of extracellular antigens and appropriated antibodies, it was shown that the treatment of the target with the mixture of biotinylated antibodies against all target components and subsequent binding with the target of biotinylated liposomes via avidin permits high liposome accumulation on the monolayer. The binding achieved is always higher than in the case of the utilization of single antibody-bearing liposomes. Besides, the system suggested is very simple and its components can be easily obtained on technological scale in standardized conditions.

L29 ANSWER 11 OF 14 MEDLINE
AN 86104393 MEDLINE
TI Fibronectin distribution in human aortic intima and atherosclerotic lesions: concentration of soluble and collagenase-releasable fractions.
AU Smith E B; Ashall C
SO BIOCHIMICA ET BIOPHYSICA ACTA, (1986 Jan 15) 880 (1) 10-5.
Journal code: A0W. ISSN: 0006-3002.
AB Fibronectin is associated with cell attachment and migration and interacts with fibrin, collagen and glycosaminoglycans; thus, it may be a factor in the focal proliferation of smooth muscle cells and collagen in atherosclerosis. We have measured, by rocket immunoelectrophoresis, the concentrations of soluble and collagenase-releasable fibronectin in normal human aortic intima and different types of atherosclerotic lesions. Soluble fibronectin concentration showed no significant difference between normal intima and lesions, but was 6-8-times higher than expected on the basis of plasma concentration and molecular mass. The concentration free in the interstitial fluid was about 3-times the expected level, suggesting that it originates from local synthesis as well as plasma insudation. In tissue, about half the fibronectin appeared to be reversibly associated with tissue components. Incubation with collagenase released fibronectin equal to twice the soluble fraction from normal intima and early proliferative lesions. In more advanced

plaques that were accumulating lipid, the amount released was significantly higher (P less than 0.05) and more than 3-times the soluble fraction, suggesting that it might be involved in lipid accumulation. However, there was no correlation between release of fibronectin and bound low-density lipoprotein.

L29 ANSWER 12 OF 14 MEDLINE
AN 84285373 MEDLINE
TI Evidence for a structural relationship between apoB75kDa and human plasma apolipoprotein B 100, from translation of human liver mRNA in vitro and immunochemical studies with monoclonal and polyclonal antibodies.
AU Bostrom K; Wettesten M; Wiklund O; Bondjers G; Lundholm K; Elias P; Norfeldt P I; Olofsson S O
SO EUROPEAN JOURNAL OF BIOCHEMISTRY, (1984 Aug 15) 143 (1) 101-7. Journal code: EMZ. ISSN: 0014-2956.
AB We have investigated the relation between an 80-kDa protein synthesized in vitro in protein-synthesizing system programmed with human liver mRNA [Olofsson, S.-O., Elias, P., Bostrom, K., Lundholm, K., Norfeldt, P.-I., Wiklund, O., Fager, G., and Bondjers, G. (1983) FEBS Lett. 156, 63-66] and a 70-80-kDa protein, apoB75kDa, isolated from the low-density lipoproteins-2 (LDL-2) [Olofson, S.-O., Bostrom, K., Svanberg, U., and Bondjers, G. (1980) Biochemistry 19, 1059-1064]. Five monoclonal antibodies directed against LDL-2 as well as polyclonal antibodies against a narrow density cut of LDL-2 (d = 1.030 - 1.055) were used to precipitate apoB-related proteins synthesized in vitro in a protein-synthesizing system programmed with human liver mRNA (or total RNA fraction). With all monoclonal antibodies as well as the polyclonal antibodies, a protein with an estimated molecular mass of 80 +/- 1.3 kDa (mean +/- SD, n = 12) could be precipitated. The observation that all monoclonal antibodies used reacted with apoB75kDa indicates a close immunological relation between this 80-kDa protein and apoB75kDa. Limited proteolysis of the 80-kDa protein (synthesized in the presence of [35S]-methionine) with Staphylococcus aureus V8 protease generated six [35S]-methionine-containing bands that could be separated on a polyacrylamide gradient gel (12-20%). All these radioactive bands corresponded to major protein-stained bands obtained after limited proteolysis of apoB75kDa. This observation suggests a structural relation between the two proteins. Taken together, our results indicate that a protein corresponding to apoB75kDa is synthesized in vitro in a protein synthesizing system programmed with human liver mRNA (or total RNA fraction). We have also compared apoB75kDa and the major component of apoLDL-2, apoB100 [Kane, J. P., Hardman, D.A., and Paulus, H.E. (1980) Proc. Natl Acad. Sci USA 77, 2465-2469] by immunochemical methods. We could demonstrate that six monoclonal antibodies directed against four to six different epitopes on LDL-2, as well as polyclonal antibodies to apoB100 and apoB75kDa, all reacted with apoB75kDa and apoB100. These

observations indicate a close immunological relation between the two proteins. Taken together our results support the hypothesis that apoB100 has a subunit structure. We therefore suggest that apoB75kDa is a subunit of apoB100 synthesized in human liver.

L29 ANSWER 13 OF 14 MEDLINE
AN 80081021 MEDLINE
TI Studies on atherogenesis and corneal transplantation using cultured vascular and corneal endothelia.
AU Gospodarowicz D; Vlodavsky I; Greenburg G; Alvarado J; Johnson L K; Moran J
SO RECENT PROGRESS IN HORMONE RESEARCH, (1979) 35 375-448. Ref: 69
Journal code: R1D. ISSN: 0079-9963.

L29 ANSWER 14 OF 14 MEDLINE
AN 79082510 MEDLINE
TI Isolation and characterization of the major lipoprotein density classes of normal and diabetic baboon (Papio anubis) plasma.
AU Bojanovski D; Alaupovic P; Kelley J L; Stout C
SO ATHEROSCLEROSIS, (1978 Dec) 31 (4) 481-7.
Journal code: 95X. ISSN: 0021-9150.

FILE 'CAPLUS' ENTERED AT 12:33:35 ON 16 MAR 2001
L30 55 S L5 AND (MOAB OR MAB OR MONOCLON?)
L31 5 S L30 AND ARTERIOSCLER?
L32 0 S L31 NOT L8

(FILE 'MEDLINE, BIOSIS, EMBASE, WPIDS, CONFSCI, SCISEARCH, JICST-EPLUS, JAPIO' ENTERED AT 12:35:08 ON 16 MAR 2001)
L33 4 S L11 AND (MOAB OR MAB OR MONOCLON?)
L34 0 S L33 NOT L15

FILE 'HOME' ENTERED AT 12:35:58 ON 16 MAR 2001

L9 ANSWER 19 OF 22 MEDLINE
AN 95194571 MEDLINE
DN 95194571 PubMed ID: 7534086
TI Immunoreactivity of apolipoprotein B-100 in oxidatively modified low density lipoprotein.
AU Valentinova N V; Gu Z W; Yang M; Yanushevskaya E V; Antonov I V; Guyton J R; Smith C V; Gotto A M Jr; Yang C Y
CS Department of Medicine, Baylor College of Medicine, Houston, Texas 77030.
NC HL-27341 (NHLBI)
HL-45619 (NHLBI)
SO BIOLOGICAL CHEMISTRY HOPPE-SEYLER, (1994 Oct) 375 (10) 651-8.
Journal code: AHC; 8503054. ISSN: 0177-3593.
CY GERMANY: Germany, Federal Republic of
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199504
ED Entered STN: 19950427
Last Updated on STN: 19970203
Entered Medline: 19950418
AB Thirteen monoclonal **antibodies** (MAbs) against apolipoprotein B-100 (apo B) were used to analyze changes in immunoreactivity of human LDL resulting from oxidation mediated by cupric ions and oxygen. Decrease in immunoreactivity of **oxidized LDL** was demonstrated by competitive ELISA with MAbs 5F8, BL3, Mb43, 2G8, B3, B5, and BL7 for which the epitopes are located within residues 1-1297, 4235-4355, 4027-4081, 3728-4306, 2239-2331, 1854-1878, and in the vicinity of residue 2331, respectively. Immunoreactivity of the epitope B6 (2239-2331) increased during first 4 hours of oxidation and then diminished gradually. Epitope B1 (405-539) had slightly reduced immunoreactivity during first 8 h of LDL oxidation and then its minor increase was observed. MAb 12G10, specific to the epitope within apo B **thrombin**-digest fragment T4 (1-1297), displayed either weak or strong binding to LDL. LDL with weak binding pattern demonstrated significant increase in immunoreactivity upon oxidation. In contrast, LDL with strong binding pattern showed little to no change. Epitopes Mb47 (3441-3569) and 8G4 (1-1297) remained unchanged in **oxidized LDL**. Immunoreactivity of apo B-100 epitope recognized by MAb 4C11 (residues 2377-2658) was shown to be a function of oxidation time: it increased progressively up to 16 h and was stabilized for another 24 h of LDL oxidation. This epitope may be unmasked by LDL oxidation and may provide a useful immunochemical marker to monitor the extent of LDL oxidation.
CT Check Tags: Human; Support, Non-U.S. Gov't; Support, U.S. Gov't, P.H.S.
Antibodies, Monoclonal: BI, biosynthesis
Antibodies, Monoclonal: IM, immunology
*Apolipoproteins B: IM, immunology
Copper: CH, chemistry
Enzyme-Linked Immunosorbent Assay
Epitopes
Lipoproteins, LDL: CH, chemistry
*Lipoproteins, LDL: IM, immunology
Oxidation-Reduction
Thiobarbituric Acid Reactive Substances: ME, metabolism
RN 7440-50-8 (Copper)
CN 0 (**Antibodies**, Monoclonal); 0 (Apolipoproteins B); 0 (Epitopes); 0 (Lipoproteins, LDL); 0 (Thiobarbituric Acid Reactive Substances); 0 (apoli

4 ANSWER 1 OF 3 BIOSIS COPYRIGHT 2001 BIOSIS
AN 1993:362524 BIOSIS
DN PREV199396048199
TI CD36 is a receptor for oxidized low density lipoprotein.
AU Endemann, Gerda (1); Stanton, Lawrence W.; Madden, Kip S.; Bryant, Carmen M.; White, R. Tyler; Protter, Andrew A.
CS (1) Scios Nova Inc., 2450 Bayshore Parkway, Mountain View, CA 94043 USA
SO Journal of Biological Chemistry, (1993) Vol. 268, No. 16, pp. 11811-11816. ISSN: 0021-9258.
DT Article
LA English
AB The oxidation of low density lipoprotein (LDL) in the arterial wall is thought to contribute to human atherosclerotic lesion formation, in part by the high affinity uptake of **oxidized LDL** (OxLDL) by macrophages, resulting in foam cell formation. We have utilized cloning by expression to identify CD36 as a macrophage receptor for OxLDL. Transfection of a CD36 clone into 293 cells results in the specific and high affinity binding of OxLDL, followed by its internalization and degradation. An anti-CD36 **antibody** blocks 50% of the binding of OxLDL to platelets and to human macrophage-like THP cells. Furthermore, like mouse macrophages, 293 cells expressing CD36 recognize LDL which has been oxidized only 4 h, whereas more extensive oxidation of the LDL is required for recognition by the other known OxLDL receptors, the acetylated LDL (AcLDL) receptor and Fc-gamma-RII-B2. CD36 may play a role in scavenging LDL modified by oxidation and may mediate effects of OxLDL on monocytes and platelets in atherosclerotic lesions.
CC Cytology and Cytochemistry - Human *02508
Biochemical Studies - Proteins, Peptides and Amino Acids 10064
Biochemical Studies - Lipids 10066
Biophysics - Membrane Phenomena *10508
Metabolism - Lipids *13006
Metabolism - Proteins, Peptides and Amino Acids *13012
Cardiovascular System - Blood Vessel Pathology *14508
Blood, Blood-Forming Organs and Body Fluids - Blood Cell Studies *15004
Blood, Blood-Forming Organs and Body Fluids - Lymphatic Tissue and Reticuloendothelial System *15008
BC Hominidae *86215
IT Major Concepts
Blood and Lymphatics (Transport and Circulation); Cardiovascular Medicine (Human Medicine, Medical Sciences); Cell Biology; Membranes (Cell Biology); Metabolism
IT Miscellaneous Descriptors
ATHEROSCLEROSIS; BASIC FIBROBLAST GROWTH FACTOR; MEMBRANE-ASSOCIATED UROKINASE-TYPE **PLASMINOGEN** ACTIVATOR; MURINE MACROPHAGE J774A.1 CELLS; PATHOGENIC FACTOR; PLASMIN GENERATION; TRANSFORMING GROWTH FACTOR-BETA
ORGN Super Taxa
Hominidae: Primates, Mammalia, Vertebrata, Chordata, Animalia
ORGN Organism Name
Hominidae (Hominidae)
ORGN Organism Superterms
animals; chordates; humans; mammals; primates; vertebrates

L4 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2001 ACS
AN 2001:62437 CAPLUS
DN 134:97520
TI Method for detecting low density lipoprotein (LDL) or denatured LDL in

5 ANSWER 1 OF 4 BIOSIS COPYRIGHT 2001 BIOSIS
AN 1996:104634 BIOSIS
DN PREV199698676769
TI Lipid islands in human gastric mucosa: Morphological and immunohistochemical findings.
AU Kaiserling, Edwin (1); Heinle, Helmut; Itabe, Hiroyuki; Takano, Tatsuya; Remmele, Wolfgang
CS (1) Inst. Pathol., Univ. Tuebingen, Liebermeisterstrasse 8, D-72076 Tuebingen Germany
SO Gastroenterology, (1996) Vol. 110, No. 2, pp. 369-374.
ISSN: 0016-5085.
DT Article
LA English
AB Background & Aims: Lipid islands are a common finding in the gastric mucosa, but their pathogenesis has not yet been established. The aim of this study was to investigate the morphology and immunophenotype of the various cells in lipid islands and to consider the possible mechanisms involved in the pathogenesis of these lesions. Methods: Morphological and immunohistochemical investigations using **antibodies** against macrophages, smooth muscle cells, and lymphocytes were performed. Unfixed tissue was available for immunostaining for low-density lipoprotein (LDL) and **oxidized LDL** in one case. Results: The lipid islands were composed of KP1-, KiM1p-, and cathepsin D-positive foam cells that were only weakly reactive for **lysozyme**. In cryostat sections, the foam cells were found to contain LDL and **oxidized LDL**. A few smooth muscle cells, plasma cells, lymphocytes, pericytes, fibroblasts, and Schwann cells that contained lipid droplets were also found. Conclusions: In gastric lipid islands, the presence of **oxidized LDL**, which is taken up by macrophages and smooth muscle cells via scavenger receptors, suggests that **oxidized LDL** is of key significance in the development and persistence of these lesions. Because the metabolism of LDL to **oxidized LDL** may occur by various mechanisms, various different initial conditions, including gastritis, may precede the development of lipid islands. Thus, anti-inflammatory treatment may be appropriate.
CC Microscopy Techniques - Histology and Histochemistry 01056
Cytology and Cytochemistry - Human *02508
Biochemical Studies - Proteins, Peptides and Amino Acids *10064
Biochemical Studies - Lipids *10066
Pathology, General and Miscellaneous - Inflammation and Inflammatory Disease 12508
Metabolism - Lipids 13006
Metabolism - Proteins, Peptides and Amino Acids 13012
Digestive System - Pathology *14006
Blood, Blood-Forming Organs and Body Fluids - Blood Cell Studies *15004
Blood, Blood-Forming Organs and Body Fluids - Lymphatic Tissue and Reticuloendothelial System *15008
Muscle - Physiology and Biochemistry *17504
Nervous System - Physiology and Biochemistry *20504
Pharmacology - Digestive System *22014
Immunology and Immunochemistry - General; Methods *34502
BC Hominidae *86215
IT Major Concepts
Biochemistry and Molecular Biophysics; Blood and Lymphatics (Transport and Circulation); Cell Biology; Gastroenterology (Human Medicine, Medical Sciences); Muscular System (Movement and Support); Nervous System (Neural Coordination); Pharmacology
IT Miscellaneous Descriptors
ANTIINFLAMMATORY DRUG THERAPY; FIBROBLASTS; FOAM CELLS; GASTRITIS; LYMPHOCYTES; OXIDIZED LOW DENSITY LIPOPROTEIN; PERICYTES; PLASMA CELLS; SCHWANN CELLS; SMOOTH MUSCLE CELLS
ORGN Super Taxa
Hominidae: Primates, Mammalia, Vertebrata, Chordata, Animalia
ORGN Organism Name
human (Hominidae)
ORGN Organism Superterms
animals; chordates; humans; mammals; primates; vertebrates